

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
4 December 2003 (04.12.2003)

PCT

(10) International Publication Number  
**WO 03/099276 A1**

(51) International Patent Classification<sup>7</sup>: **A61K 31/41**,  
31/44, 31/435, C07D 213/14, 213/75, 471/04, 514/300,  
514/303, 514/352, 514/406, 514/407, 546/117, 546/119,  
546/309, 548/364, 548/369, 548/369

(21) International Application Number: PCT/US03/13893

(22) International Filing Date: 5 May 2003 (05.05.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/379,357 10 May 2002 (10.05.2002) US  
60/415,367 2 October 2002 (02.10.2002) US

(71) Applicant (*for all designated States except US*): **BRISTOL-MYERS SQUIBB COMPANY** [US/US]; P.O. BOX 4000, ROUTE 206 and PROVINCELINE ROAD, PRINCETON, NJ 08543-4000 (US).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **QIAO, Jennifer, X.** [CN/US]; 3233 Town Court South, Lawrenceville, NJ 08648 (US). **PINTO, Donald, J.** [US/US]; 425 Brentford Road, Kennett Square, PA 19348 (US). **ORWAT, Michael, J.** [US/US]; 118 S. Colts Neck Way, Hockessin, DE 19707

(US). **HAN, Wei** [CN/US]; 660 ROSALIND RUN, Yardley, PA 19067 (US). **FRIEDRICH, Sarah, R.** [US/US]; 1906 Cherrie Circle, Blue Bell, PA 19422 (US).

(74) Agents: **BELFIELD, Jing, S.** et al.; Bristol-Myers Squibb Company, P.O. Box 4000, Route 206 and Provinceline Road, Princeton, NJ 08543-4000 (US).

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: 1,1-DISUBSTITUTED CYCLOALKYL DERIVATIVES AS FACTOR XA INHIBITORS

(57) Abstract: The present application describes 1,1-disubstituted cycloalkyl compounds and derivatives thereof, or pharmaceutically acceptable salt forms thereof, which are useful as inhibitors of factor Xa.



WO 03/099276 A1

## TITLE

1,1-Disubstituted Cycloalkyl Derivatives As Factor Xa  
Inhibitors

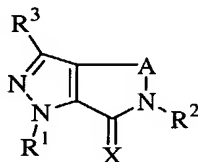
5

## FIELD OF THE INVENTION

This invention relates generally to 1,1-disubstituted cycloalkyl compounds, which are inhibitors of trypsin-like serine protease enzymes, especially factor Xa,  
 10 pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

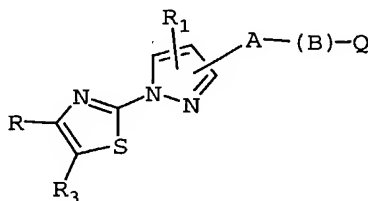
## BACKGROUND OF THE INVENTION

15 U.S. Patent Nos. 3,365,459, 3,340,269, and 3,423,414 illustrate anti-inflammatory inhibitors of the following formula:



wherein A is 2-3 carbon atoms, X can be O, and R<sup>1</sup> and R<sup>3</sup> can  
 20 be substituted or unsubstituted aromatic groups. None of these patents, however, exemplify or suggest compounds of the present invention.

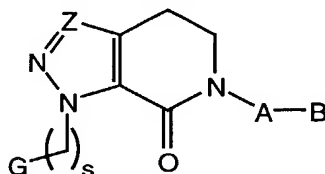
US 5,342,851 depicts thiazole platelet aggregation inhibitors including those of the following formula:



25

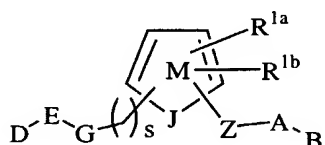
wherein A is a linker, B can be a linker or a ring, Q is a ring or an amino group, R, R<sub>1</sub>, and R<sub>3</sub> are a variety of groups. This patent, however, does not exemplify or suggest compounds of the present invention.

WO00/39131 describes heterobicyclic Factor Xa inhibitors of which the following is an example formula:



wherein Z is C or N, G is a mono- or bicyclic group, A is a cyclic moiety and B is a basic group or a cyclic moiety. Compounds specifically described in WO00/39131 are not considered to be part of the present invention.

WO98/28269, WO98/28282, WO99/32454, US 6,020,357, and US 6,271,237 describe Factor Xa inhibitors of the following formula:



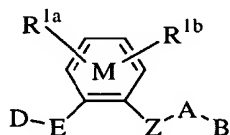
wherein ring M is a heterocycle, Z is a linker, A is a ring, B is a basic or cyclic group, D is a basic moiety, and E is a ring. Compounds specifically described in WO98/28269, WO98/28282, WO99/32454, US 6,020,357, and US 6,271,237 are not considered to be part of the present invention.

WO98/57951 describes Factor Xa inhibitors of the following formula:



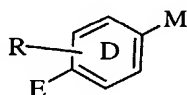
wherein ring M can be a variety of heterocycles and rings D-E represent a heterobicyclic group. Compounds specifically described in WO98/57951 are not considered to be part of the present invention.

WO98/57934 and US 6,060,491 describe Factor Xa inhibitors of the following formula:



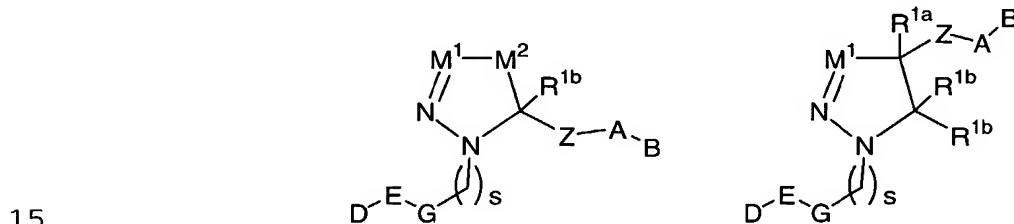
wherein ring M is a 6-membered heteroaryl, Z is a linker, A is a ring, B is a basic or cyclic group, D is a basic moiety, and E is a ring. Compounds specifically described in WO98/57934 and US 6,060,491 are not considered to be  
 5 part of the present invention.

WO98/57937 and US 5,998,424 describe Factor Xa inhibitors of the following formula:



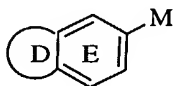
wherein ring M is a variety of rings, ring D is an aromatic  
 10 ring, and R and E are non-basic groups. Compounds specifically described in WO98/57937 and US 5,998,424 are not considered to be part of the present invention.

WO99/50255 and US 6,191,159 describe pyrazoline and triazoline Factor Xa inhibitors of the following formulas:



Compounds specifically described in WO99/50255 and US 6,191,159 are not considered to be part of the present invention.

WO00/59902 describes Factor Xa inhibitors of the  
 20 following formula:

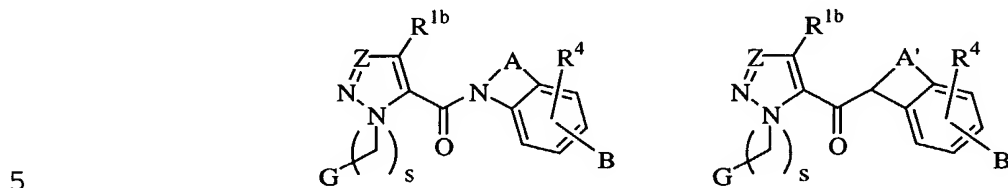


wherein ring M can be a variety of rings all of which are substituted with Z-A-B, Z is a linker, A is a ring, B is a sulfonyl-containing heterobicycle, and rings D-E represent  
 25 a heterobicyclic group or a 6-membered ring. Compounds specifically described in WO00/59902 are not considered to be part of the present invention.

WO01/32628 describes cyano-pyrroles, cyano-imidazoles, cyano-pyrazoles, and cyano-triazoles that are Factor Xa

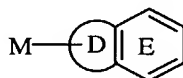
inhibitors. Compounds specifically described in WO01/32628 are not considered to be part of the present invention.

WO01/05784 describes Factor Xa inhibitors of the following formulas:



wherein Z is C or N, G is a mono- or bicyclic ring M, A is a linker, B is a basic or cyclic group. Compounds specifically described in WO01/05784 are not considered to be part of the present invention.

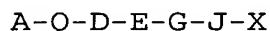
10 WO00/39108 describes Factor Xa inhibitors of the following formula:



wherein ring M can be a variety of heterocycles and rings D-E represent a heterobicyclic group. Compounds

15 specifically described in WO00/39108 are not considered to be part of the present invention.

WO01/19798 describes factor Xa inhibitors of the following formula:



20 wherein A, D, G, and X can be phenyl or heterocycle. However, none of the presently claimed compounds are exemplified or suggested in WO01/19798.

Activated factor Xa, whose major practical role is the generation of thrombin by the limited proteolysis of prothrombin, holds a central position that links the intrinsic and extrinsic activation mechanisms in the final common pathway of blood coagulation. The generation of thrombin, the final serine protease in the pathway to generate a fibrin clot, from its precursor is amplified by formation of prothrombinase complex (factor Xa, factor V, Ca<sup>2+</sup> and phospholipid). Since it is calculated that one molecule of factor Xa can generate 138 molecules of

25

30

thrombin (Elodi, S., Varadi, K.: Optimization of conditions for the catalytic effect of the factor IXa-factor VIII Complex: Probable role of the complex in the amplification of blood coagulation. *Thromb. Res.* **1979**, 15, 617-629),  
5 inhibition of factor Xa may be more efficient than inactivation of thrombin in interrupting the blood coagulation system.

Therefore, efficacious and specific inhibitors of factor Xa are needed as potentially valuable therapeutic  
10 agents for the treatment of thromboembolic disorders. It is thus desirable to discover new factor Xa inhibitors. In addition, it is also desirable to find new compounds with improved pharmacological characteristics compared with known factor Xa inhibitors. For example, it is preferred  
15 to find new compounds with improved factor Xa inhibitory activity and selectivity for factor Xa versus other serine proteases (i.e., trypsin). It is also desirable and preferable to find compounds with advantageous and improved characteristics in one or more of the following categories,  
20 but are not limited to: (a) pharmaceutical properties; (b) dosage requirements; (c) factors which decrease blood concentration peak-to-trough characteristics; (d) factors that increase the concentration of active drug at the receptor; (e) factors that decrease the liability for  
25 clinical drug-drug interactions; (f) factors that decrease the potential for adverse side-effects; and, (g) factors that improve manufacturing costs or feasibility.

#### SUMMARY OF THE INVENTION

30 Accordingly, the present invention provides novel 1,1-disubstituted cycloalkyl compounds that are useful as factor Xa inhibitors or pharmaceutically acceptable salts or prodrugs thereof.

The present invention provides pharmaceutical  
35 compositions comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of at least

one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

The present invention provides a method for treating thromboembolic disorders comprising administering to a host  
5 in need of such treatment a therapeutically effective amount of at least one of the compounds of the present invention or a pharmaceutically acceptable salt or prodrug form thereof.

The present invention provides a novel method of  
10 treating a patient in need of thromboembolic disorder treatment, comprising: administering a compound of the present invention or a pharmaceutically acceptable salt thereof in an amount effective to treat a thromboembolic disorder.

15 The present invention provides a novel method, comprising: administering a compound of the present invention or a pharmaceutically acceptable salt thereof in an amount effective to treat a thromboembolic disorder.

The present invention provides novel compounds for use  
20 in therapy.

The present invention provides the use of novel compounds for the manufacture of a medicament for the treatment of a thromboembolic disorder.

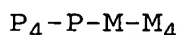
These and other objects, which will become apparent  
25 during the following detailed description, have been achieved by the inventors' discovery that the presently claimed 1,1-disubstituted cycloalkyl compounds, or pharmaceutically acceptable salt or prodrug forms thereof, are effective factor Xa inhibitors.

30

#### DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

[1] In an embodiment, the present invention provides a novel compound of formula I:

35



I

6

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

M is a 3-10 membered carbocycle or a 4-10 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)<sub>p</sub>, N, and NZ<sup>2</sup>;

ring M is substituted with 0-3 R<sup>1a</sup> and 0-2 carbonyl groups, and there are 0-3 ring double bonds;

10

P is fused onto ring M and is a 5, 6, or 7 membered carbocycle or a 5, 6, or 7 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)<sub>p</sub>, and N;

15

ring P is substituted with 0-3 R<sup>1a</sup> and 0-2 carbonyl groups, and there are 0-3 ring double bonds;

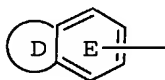
20

alternatively, ring P is absent and P<sub>4</sub> is directly attached to ring M, provided that when ring P is absent, P<sub>4</sub> and M<sub>4</sub> are attached to the 1,2, 1,3, or 1,4 positions of ring M;

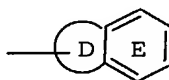
25

one of P<sub>4</sub> and M<sub>4</sub> is -Z-A-B and the other -G<sub>1</sub>-G, provided that P<sub>4</sub> and M<sub>4</sub> are attached to different rings when ring P is present;

G is a group of formula IIa or IIb:



IIa



IIb

30

ring D, including the two atoms of Ring E to which it is attached, is a 5-6 membered ring consisting of carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;



ring D is substituted with 0-2 R and there are 0-3 ring double bonds;

- 5 E is selected from phenyl, pyridyl, pyrimidyl, pyrazinyl, and pyridazinyl, and is substituted with 1-3 R;

alternatively, ring D is absent and ring E is selected from phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, triazolyl, thienyl, and thiazolyl, and ring E is substituted with 1-3 R;

alternatively, ring D is absent and ring E is selected from phenyl, pyridyl, pyrimidyl, pyrazinyl, pyridazinyl, pyrrolyl, pyrazolyl, imidazolyl, isoxazolyl, oxazolyl, triazolyl, thienyl, and thiazolyl, and ring E is substituted with 1 R and with a 5-6 membered heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, wherein the 5-6 membered heterocycle is substituted with 0-2 carbonyls and 1-3 R and there are 0-3 ring double bonds;

- 25 R is selected from H, C<sub>1-4</sub> alkyl, F, Cl, Br, I, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CN, C(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NHC(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, ONHC(=NR<sup>8</sup>)NR<sup>7</sup>R<sup>9</sup>, NR<sup>8</sup>CH(=NR<sup>7</sup>), NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)H, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)R<sup>2c</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>C(O)R<sup>7</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>OR<sup>3</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>S(O)<sub>p</sub>NR<sup>7</sup>R<sup>8</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>S(O)<sub>p</sub>R<sup>7</sup>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>SR<sup>3</sup>,

$(\text{CR}^8\text{R}^9)_t\text{S}(\text{O})\text{R}^3$ ,  $(\text{CR}^8\text{R}^9)_t\text{S}(\text{O})_2\text{R}^3$ , and  $\text{OCF}_3$ , provided that  $\text{S}(\text{O})_p\text{R}^7$  forms other than  $\text{S}(\text{O})_2\text{H}$  or  $\text{S}(\text{O})\text{H}$ ;

alternatively, when 2 R groups are attached to adjacent  
 5 atoms, they combine to form methylenedioxy or ethylenedioxy;

A is selected from:

$\text{C}_{3-10}$  carbocycle substituted with 0-2  $\text{R}^4$ , and  
 10 5-12 membered heterocycle substituted with 0-2  $\text{R}^4$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $\text{S}(\text{O})_p$ ;

B is  $\text{Y-R}^{4a}$  or  $\text{X-Y-R}^{4a}$ , provided that Z and B are attached to  
 15 different atoms on A and A and  $\text{R}^{4a}$  or X and  $\text{R}^{4a}$  are attached to the same atom on Y;

X is selected from  $-(\text{CR}^2\text{R}^{2a})_{1-4}-$ ,  $-\text{CR}^2(\text{CR}^2\text{R}^{2b})(\text{CH}_2)_t-$ ,  
 $-\text{C}(\text{O})-$ ,  $-\text{C}(=\text{NR}^{1b})-$ ,  $-\text{CR}^2(\text{NR}^{1b}\text{R}^2)-$ ,  $-\text{CR}^2(\text{OR}^2)-$ ,  
 20  $-\text{CR}^2(\text{SR}^2)-$ ,  $-\text{C}(\text{O})\text{CR}^2\text{R}^{2a}-$ ,  $-\text{CR}^2\text{R}^{2a}\text{C}(\text{O})-$ ,  $-\text{S}(\text{O})-$ ,  $-\text{S}(\text{O})_2-$ ,  
 $-\text{SCR}^2\text{R}^{2a}-$ ,  $-\text{S}(\text{O})\text{CR}^2\text{R}^{2a}-$ ,  $-\text{S}(\text{O})_2\text{CR}^2\text{R}^{2a}-$ ,  $-\text{CR}^2\text{R}^{2a}\text{S}-$ ,  
 $-\text{CR}^2\text{R}^{2a}\text{S}(\text{O})-$ ,  $-\text{CR}^2\text{R}^{2a}\text{S}(\text{O})_2-$ ,  $-\text{S}(\text{O})_2\text{NR}^2-$ ,  
 $-\text{S}(\text{O})_2\text{NR}^2\text{CR}^2\text{R}^{2a}-$ ,  $-\text{CR}^2\text{R}^{2a}\text{S}(\text{O})_2\text{NR}^2-$ ,  $-\text{NR}^2\text{S}(\text{O})_2-$ ,  
 $-\text{CR}^2\text{R}^{2a}\text{NR}^2\text{S}(\text{O})_2-$ ,  $-\text{NR}^2\text{S}(\text{O})_2\text{CR}^2\text{R}^{2a}-$ ,  $-\text{NR}^2\text{C}(\text{O})-$ ,  
 25  $-\text{C}(\text{O})\text{NR}^2-$ ,  $-\text{NR}^2\text{C}(\text{O})\text{CR}^2\text{R}^{2a}-$ ,  $-\text{C}(\text{O})\text{NR}^2\text{CR}^2\text{R}^{2a}-$ ,  
 $-\text{CR}^2\text{R}^{2a}\text{NR}^2\text{C}(\text{O})-$ ,  $-\text{CR}^2\text{R}^{2a}\text{C}(\text{O})\text{NR}^2-$ ,  $\text{NR}^2$ ,  $-\text{NR}^2\text{CR}^2\text{R}^{2a}-$ ,  
 $-\text{CR}^2\text{R}^{2a}\text{NR}^2-$ , O,  $-\text{OCR}^2\text{R}^{2a}-$ , and  $-\text{CR}^2\text{R}^{2a}\text{O}-$ ;

Y is a  $\text{C}_{3-10}$  carbocycle or 3-10 membered heterocycle,  
 30 wherein the carbocycle or heterocycle consists of carbon atoms and 0-4 heteroatoms selected from N, O, and  $\text{S}(\text{O})_p$ , the carbocycle or heterocycle further comprises 0-4 double bonds and 0-2 carbonyl groups, and the carbocycle or heterocycle is substituted with

0-2 R<sup>4</sup>, provided that Y is other than a 1,3-dioxolanyl group;

alternatively, Y is CY<sup>1</sup>Y<sup>2</sup>, and Y<sup>1</sup> and Y<sup>2</sup> are independently  
 5 C<sub>1-4</sub> alkyl substituted with 0-2 R<sup>4</sup>;

G<sub>1</sub> is absent or is selected from (CR<sup>3</sup>R<sup>3a</sup>)<sub>1-5</sub>,

(CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>CR<sup>3</sup>=CR<sup>3</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>C≡C(CR<sup>3</sup>R<sup>3a</sup>)<sub>0-2</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 10 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>OC(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>OC(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>C(O)O(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>C(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 15 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>C(S)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>S(O)<sub>2</sub>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>S(O)<sub>2</sub>NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3e</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 20 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 25 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3bb</sup>C(S)(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>NR<sup>3b</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(S)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)NR<sup>3b</sup>C(O)(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>,  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>C(O)NR<sup>3b</sup>S(O)<sub>2</sub>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, and  
 (CR<sup>3</sup>R<sup>3a</sup>)<sub>u</sub>S(O)<sub>2</sub>NR<sup>3b</sup>C(O)NR<sup>3b</sup>(CR<sup>3</sup>R<sup>3a</sup>)<sub>w</sub>, wherein u + w total  
 30 0, 1, 2, 3, or 4, provided that G<sub>1</sub> does not form a N-S, NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond with either group to which it is attached;

Z is selected from a bond,  $-(CR^3R^{3e})_{1-4}-$ ,  
 $(CR^3R^{3e})_qO(CR^3R^{3e})_{q1}$ ,  $(CR^3R^{3e})_qNR^{3b}(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qC(O)(CR^3R^{3e})_{q1}$ ,  $(CR^3R^{3e})_qC(O)O(CR^3R^{3e})_{q1}$ ,  
5  $(CR^3R^{3e})_qOC(O)(CR^3R^{3e})_{q1}$ ,  $(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qNR^{3b}C(O)(CR^3R^{3e})_{q1}$ ,  $(CR^3R^{3e})_qOC(O)O(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qOC(O)NR^{3b}(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qNR^{3b}C(O)O(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qNR^{3b}C(O)NR^{3b}(CR^3R^{3e})_{q1}$ ,  
10  $(CR^3R^{3e})_qC(O)(CR^3R^{3e})_qC(O)(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qNR^{3b}(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qNR^{3b}C(O)(CR^3R^{3e})_qC(O)(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qC(O)(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qNR^{3b}C(O)(CR^3R^{3e})_qC(O)NR^{3b}(CR^3R^{3e})_{q1}$ ,  
15  $(CR^3R^{3e})_qS(CR^3R^{3e})_{q1}$ ,  $(CR^3R^{3e})_qS(O)(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qS(O)_2(CR^3R^{3e})_{q1}$ ,  $(CR^3R^{3e})_qSO_2NR^{3b}(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qNR^{3b}SO_2(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qS(O)NR^{3b}C(O)(CR^3R^{3e})_{q1}$ ,  
 $(CR^3R^{3e})_qC(O)NR^{3b}S(O)_2(CR^3R^{3e})_{q1}$ , and  
20  $(CR^3R^{3e})_qNR^{3b}SO_2NR^{3b}(CR^3R^{3e})_{q1}$ , wherein  $q + q1$  total 0,  
1, 2, 3, or 4, provided that Z does not form a N-S,  
NCH<sub>2</sub>N, NCH<sub>2</sub>O, or NCH<sub>2</sub>S bond with either group to which  
it is attached;

25 provided that:

(a) when ring P is absent and ring M is a pyridyl  
ring, then Z is other than C(O)NHCH<sub>2</sub>; and,

(b) when ring P is absent and ring M is a piperazinyl  
ring, then either Z is other than alkylene or A is other  
30 than phenyl;

Z<sup>2</sup> is selected from H, S(O)<sub>2</sub>NHR<sup>3b</sup>, C(O)R<sup>3b</sup>, C(O)NHR<sup>3b</sup>,  
C(O)OR<sup>3f</sup>, S(O)R<sup>3f</sup>, S(O)<sub>2</sub>R<sup>3f</sup>, C<sub>1-6</sub> alkyl substituted with

0-2 R<sup>1a</sup>, C<sub>2-6</sub> alkenyl substituted with 0-2 R<sup>1a</sup>, C<sub>2-6</sub>  
 alkynyl substituted with 0-2 R<sup>1a</sup>, -(C<sub>0-4</sub> alkyl)-C<sub>3-10</sub>  
 carbocycle substituted with 0-3 R<sup>1a</sup>, and -(C<sub>0-4</sub> alkyl)-  
 5-10 membered heterocycle substituted with 0-3 R<sup>1a</sup> and  
 5 consisting of: carbon atoms and 1-4 heteroatoms  
 selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>1a</sup>, at each occurrence, is selected from H, -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-R<sup>1b</sup>,  
 -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-CR<sup>3</sup>R<sup>1b</sup>R<sup>1b</sup>, -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-O-(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-R<sup>1b</sup>,  
 10 -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-NR<sup>2</sup>-(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-R<sup>1b</sup>,  
 -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-S(O)<sub>p</sub>-(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-R<sup>1b</sup>,  
 -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-CO<sub>2</sub>-(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-R<sup>1b</sup>,  
 -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-C(O)NR<sup>2</sup>-(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-R<sup>1b</sup>,  
 -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-C(O)-(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-R<sup>1b</sup>, -C<sub>2-6</sub> alkenylene-R<sup>1b</sup>,  
 15 -C<sub>2-6</sub> alkynylene-R<sup>1b</sup>, and -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-C(=NR<sup>1b</sup>)NR<sup>3</sup>R<sup>1b</sup>,  
 provided that R<sup>1a</sup> forms other than an N-halo, N-S, O-O,  
 or N-CN bond;

alternatively, when two R<sup>1a</sup> groups are attached to adjacent  
 20 atoms or to the same carbon atom, together with the  
 atoms to which they are attached, they form a 5-7  
 membered ring consisting of: carbon atoms and 0-2  
 heteroatoms selected from the group consisting of N,  
 O, and S(O)<sub>p</sub>, this ring being substituted with 0-2 R<sup>4b</sup>  
 25 and comprising: 0-3 double bonds;

R<sup>1b</sup> is selected from H, C<sub>1-3</sub> alkyl, F, Cl, Br, I, -CN, -NO<sub>2</sub>,  
 -CHO, (CF<sub>2</sub>)<sub>r</sub>CF<sub>3</sub>, (CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>OR<sup>2</sup>, NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2b</sup>, CO<sub>2</sub>R<sup>2b</sup>,  
 OC(O)R<sup>2</sup>, CH(CH<sub>2</sub>OR<sup>2</sup>)<sub>2</sub>, (CF<sub>2</sub>)<sub>r</sub>CO<sub>2</sub>R<sup>2a</sup>, S(O)<sub>p</sub>R<sup>2b</sup>,  
 30 NR<sup>2</sup>(CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, C(=NR<sup>2c</sup>)NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>,  
 NR<sup>2</sup>C(O)<sub>2</sub>R<sup>2a</sup>, OC(O)NR<sup>2</sup>R<sup>2a</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, C(O)NR<sup>2</sup>(CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>,  
 SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>R<sup>2</sup>, C(O)NR<sup>2</sup>SO<sub>2</sub>R<sup>2</sup>, C<sub>3-6</sub> carbocycle  
 substituted with 0-2 R<sup>4b</sup>, and 5-10 membered heterocycle

substituted with 0-2  $R^{4b}$  and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , provided that  $R^{1b}$  forms other than an O-O, N-halo, N-S, or N-CN bond and  
5 provided that  $S(O)_pR^2$  forms other than  $S(O)_2H$  or  $S(O)H$ ;

$R^2$ , at each occurrence, is selected from H,  $CF_3$ ,  $C_{1-6}$  alkyl, benzyl,  $-(CH_2)_r-C_{3-10}$  carbocycle substituted with 0-2  $R^{4b}$ , and  $-(CH_2)_r-5-10$  membered heterocycle substituted  
10 with 0-2  $R^{4b}$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;

$R^{2a}$ , at each occurrence, is selected from H,  $CF_3$ ,  $C_{1-6}$   
15 alkyl, benzyl,  $-(CH_2)_r-C_{3-10}$  carbocycle substituted with 0-2  $R^{4b}$ , and  $-(CH_2)_r-5-10$  membered heterocycle substituted with 0-2  $R^{4b}$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;

20 alternatively,  $R^2$  and  $R^{2a}$ , together with the nitrogen atom to which they are attached, combine to form a 3-6 membered saturated, partially saturated or unsaturated ring substituted with 0-2  $R^{4b}$  and consisting of: 0-1  
25 additional heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;

$R^{2b}$ , at each occurrence, is selected from  $CF_3$ ,  $C_{1-4}$  alkoxy substituted with 0-2  $R^{4b}$ ,  $C_{1-6}$  alkyl substituted with  
30 0-3  $R^{4b}$ ,  $-(CH_2)_r-C_{3-10}$  carbocycle substituted with 0-2  $R^{4b}$ , and  $-(CH_2)_r-5-10$  membered heterocycle substituted with 0-2  $R^{4b}$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;

- $R^{2c}$ , at each occurrence, is selected from  $CF_3$ , OH,  $C_{1-4}$  alkoxy,  $C_{1-6}$  alkyl,  $-(CH_2)_r-C_{3-10}$  carbocycle substituted with 0-2  $R^{4b}$ , and  $-(CH_2)_r-5-10$  membered heterocycle substituted with 0-2  $R^{4b}$  and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;
- $R^{2d}$ , at each occurrence, is selected from H,  $R^{4c}$ ,  $C_{1-6}$  alkyl substituted with 0-2  $R^{4c}$ ,  $-(CR^3R^{3a})_r-C_{3-10}$  carbocycle substituted with 0-2  $R^{4c}$ , and  $-(CR^3R^{3a})_r-5-10$  membered heterocycle substituted with 0-2  $R^{4c}$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , provided that  $R^{2d}$  forms other than a N-halo, N-C-halo,  $S(O)_p$ -halo, O-halo, N-S, S-N,  $S(O)_p-S(O)_p$ , S-O, O-N, O-S, or O-O moiety;
- alternatively, when two  $R^{2d}$ 's are attached to the same nitrogen atom, then  $R^{2d}$  and  $R^{2d}$ , together with the nitrogen atom to which they are attached, combine to form a 5-10 membered saturated, partially saturated or unsaturated ring substituted with 0-2  $R^{4b}$  and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;
- $R^{2e}$ , at each occurrence, is selected from H,  $R^{4c}$ ,  $C_{1-6}$  alkyl substituted with 0-2  $R^{4c}$ ,  $-(CR^3R^{3a})_r-C_{3-10}$  carbocycle substituted with 0-2  $R^{4c}$ , and  $-(CR^3R^{3a})_r-5-10$  membered heterocycle substituted with 0-2  $R^{4c}$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , provided that  $R^{2e}$  forms other than a C(O)-halo or C(O)- $S(O)_p$  moiety;

$R^3$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH_2CH_2CH_2CH_3$ ,  $CH_2CH(CH_3)_2$ ,  $CH(CH_3)CH_2CH_3$ ,  $C(CH_3)_3$ , benzyl, and phenyl;

5  $R^{3a}$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH_2CH_2CH_2CH_3$ ,  $CH_2CH(CH_3)_2$ ,  $CH(CH_3)CH_2CH_3$ ,  $C(CH_3)_3$ , benzyl, and phenyl;

alternatively,  $R^3$  and  $R^{3a}$ , together with the nitrogen atom  
10 to which they are attached, combine to form a 5 or 6  
membered saturated, partially unsaturated, or  
unsaturated ring consisting of: carbon atoms, the  
nitrogen atom to which  $R^3$  and  $R^{3a}$  are attached, and 0-1  
additional heteroatoms selected from the group  
15 consisting of N, O, and  $S(O)_p$ ;

$R^{3b}$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl  
substituted with 0-2  $R^{1a}$ ,  $C_{2-6}$  alkenyl substituted with  
0-2  $R^{1a}$ ,  $C_{2-6}$  alkynyl substituted with 0-2  $R^{1a}$ ,  $-(C_{0-4}$   
20 alkyl)-5-10 membered carbocycle substituted with 0-3  
 $R^{1a}$ , and  $-(C_{0-4}$  alkyl)- 5-10 membered heterocycle  
substituted with 0-3  $R^{1a}$  and consisting of: carbon  
atoms and 1-4 heteroatoms selected from the group  
consisting of N, O, and  $S(O)_p$ ;

25

$R^{3c}$ , at each occurrence, is selected from  $CH_3$ ,  $CH_2CH_3$ ,  
 $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH_2CH_2CH_2CH_3$ ,  $CH_2CH(CH_3)_2$ ,  
 $CH(CH_3)CH_2CH_3$ ,  $C(CH_3)_3$ , benzyl, and phenyl;

30  $R^{3d}$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  
 $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH_2CH_2CH_2CH_3$ ,  $CH_2CH(CH_3)_2$ ,  
 $CH(CH_3)CH_2CH_3$ ,  $C_{1-4}$  alkyl-phenyl, and  $C(=O)R^{3c}$ ;



- $R^{3e}$ , at each occurrence, is selected from H,  $S(O)_2NHR^3$ ,  
 $C(O)R^3$ ,  $C(O)NHR^3$ ,  $C(O)OR^{3f}$ ,  $S(O)R^{3f}$ ,  $S(O)_2R^{3f}$ ,  $C_{1-6}$   
 alkyl substituted with 0-2  $R^{1a}$ ,  $C_{2-6}$  alkenyl  
 substituted with 0-2  $R^{1a}$ ,  $C_{2-6}$  alkynyl substituted with  
 5 0-2  $R^{1a}$ ,  $-(C_{0-4} \text{ alkyl})$ -5-10 membered carbocycle  
 substituted with 0-3  $R^{1a}$ , and  $-(C_{0-4} \text{ alkyl})$ - 5-10  
 membered heterocycle substituted with 0-3  $R^{1a}$  and  
 consisting of: carbon atoms and 1-4 heteroatoms  
 selected from the group consisting of N, O, and  $S(O)_p$ ;  
 10
- $R^{3f}$ , at each occurrence, is selected from:  $C_{1-6}$  alkyl  
 substituted with 0-2  $R^{1a}$ ,  $C_{2-6}$  alkenyl substituted with  
 0-2  $R^{1a}$ ,  $C_{2-6}$  alkynyl substituted with 0-2  $R^{1a}$ ,  $-(C_{0-4}$   
 alkyl)-5-10 membered carbocycle substituted with 0-3  
 15  $R^{1a}$ , and  $-(C_{0-4} \text{ alkyl})$ -5-10 membered heterocycle  
 substituted with 0-3  $R^{1a}$  and consisting of: carbon  
 atoms and 1-4 heteroatoms selected from the group  
 consisting of N, O, and  $S(O)_p$ ;  
 20
- $R^{3g}$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  
 $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH_2CH_2CH_2CH_3$ ,  $CH_2CH(CH_3)_2$ ,  
 $CH(CH_3)CH_2CH_3$ ,  $C(CH_3)_3$ ,  $-(CH_2)_r$ -3-6 membered  
 carbocycle, and  $-(CH_2)_r$ -5-6 membered heterocycle  
 consisting of: carbon atoms and 1-4 heteroatoms  
 25 selected from the group consisting of N, O, and  $S(O)_p$ ;  
 30

alternatively, when  $R^3$  and  $R^{3g}$  are attached to the same  
 carbon atom, they combine with the attached carbon  
 atom to form a cyclopropyl group;

30

$R^4$ , at each occurrence, is selected from H, =O,  
 $(CR^3R^{3a})_rOR^2$ , F, Cl, Br, I,  $C_{1-4}$  alkyl,  $(CR^3R^{3a})_rCN$ ,  
 $(CR^3R^{3a})_rNO_2$ ,  $(CR^3R^{3a})_rNR^2R^{2a}$ ,  $(CR^3R^{3a})_rC(O)R^{2c}$ ,

$(CR^3R^{3a})_rNR^2C(O)R^{2b}$ ,  $(CR^3R^{3a})_rC(O)NR^2R^{2a}$ ,  
 $(CR^3R^{3a})_rNR^2C(O)NR^2R^{2a}$ ,  $(CR^3R^{3a})_rC(=NR^2)NR^2R^{2a}$ ,  
 $(CR^3R^{3a})_rC(=NS(O)_2R^{5a})NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2C(=NR^2)NR^2R^{2a}$ ,  
 $(CR^3R^{3a})_rC(O)NR^2C(=NR^2)NR^2R^{2a}$ ,  $(CR^3R^{3a})_rSO_2NR^2R^{2a}$ ,  
5  $(CR^3R^{3a})_rNR^2SO_2NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2SO_2-C_{1-4}$  alkyl,  
 $(CR^3R^{3a})_rNR^2SO_2R^{5a}$ ,  $(CR^3R^{3a})_rS(O)_pR^{5a}$ ,  $(CR^3R^{3a})_r(CF_2)_rCF_3$ ,  
 $N(CH_2)_rR^{1b}$ ,  $O(CH_2)_rR^{1b}$ ,  $S(CH_2)_rR^{1b}$ ,  $(CR^3R^{3a})_{r-5-6}$   
membered carbocycle substituted with 0-1  $R^5$ , and a  
 $(CR^3R^{3a})_{r-5-6}$  membered heterocycle substituted with 0-1  
10  $R^5$  and consisting of: carbon atoms and 1-4  
heteroatoms selected from the group consisting of N,  
O, and  $S(O)_p$ ;

$R^{4a}$  is selected from  $C_{1-6}$  alkyl substituted with 0-2  $R^{4c}$ ,  
15  $C_{2-6}$  alkenyl substituted with 0-2  $R^{4c}$ ,  $C_{2-6}$  alkynyl  
substituted with 0-2  $R^{4c}$ ,  $-(CR^3R^{3g})_r-C_{5-10}$  membered  
carbocycle substituted with 0-3  $R^{4c}$ ,  $-(CR^3R^{3g})_{r-5-10}$   
membered heterocycle substituted with 0-3  $R^{4c}$  and  
consisting of: carbon atoms and 1-4 heteroatoms  
20 selected from the group consisting of N, O, and  $S(O)_p$ ,  
 $(CR^3R^{3g})_rCN$ ,  $(CR^3R^{3g})_rC(=NR^{2d})NR^{2d}R^{2d}$ ,  
 $(CR^3R^{3g})_rNR^{2d}C(=NR^{2d})NR^{2d}R^{2d}$ ,  $(CR^3R^{3g})_rNR^{2d}C(R^{2e})(=NR^{2d})$ ,  
 $(CR^3R^{3g})_rNR^{2d}R^{2d}$ ,  $(CR^3R^{3g})_rN(\rightarrow O)R^{2d}R^{2d}$ ,  $(CR^3R^{3g})_rOR^{2d}$ ,  
 $(CR^3R^{3g})_r-NR^{2d}C(O)R^{2e}$ ,  $(CR^3R^{3g})_r-C(O)R^{2e}$ ,  
25  $(CR^3R^{3g})_r-OC(O)R^{2e}$ ,  $(CR^3R^{3g})_r-C(O)NR^{2d}R^{2d}$ ,  
 $(CR^3R^{3g})_r-C(O)OR^{2d}$ ,  $(CR^3R^{3g})_r-NR^{2d}C(O)NR^{2d}R^{2d}$ ,  
 $(CR^3R^{3g})_r-OC(O)NR^{2d}R^{2d}$ ,  $(CR^3R^{3g})_r-NR^{2d}C(O)OR^{2d}$ ,  
 $(CR^3R^{3g})_r-SO_2NR^{2d}R^{2d}$ ,  $(CR^3R^{3g})_r-NR^{2d}SO_2NR^{2d}R^{2d}$ ,  
 $(CR^3R^{3g})_r-C(O)NR^{2d}SO_2R^{2d}$ ,  $(CR^3R^{3g})_r-NR^{2d}SO_2R^{2d}$ , and  
30  $(CR^3R^{3g})_r-S(O)_pR^{2d}$ , provided that  $S(O)_pR^{2d}$  forms other  
than  $S(O)_2H$  or  $S(O)H$  and further provided that  $R^{4a}$  is  
other than a hydroxamic acid;

$R^{4b}$ , at each occurrence, is selected from H, =O,  $(CH_2)_rOR^3$ ,  
 $(CH_2)_rF$ ,  $(CH_2)_rCl$ ,  $(CH_2)_rBr$ ,  $(CH_2)_rI$ ,  $C_{1-4}$  alkyl,  
 $(CH_2)_rCN$ ,  $(CH_2)_rNO_2$ ,  $(CH_2)_rNR^3R^{3a}$ ,  $(CH_2)_rC(O)R^3$ ,  
5  $(CH_2)_rC(O)OR^{3c}$ ,  $(CH_2)_rNR^3C(O)R^{3a}$ ,  $(CH_2)_r-C(O)NR^3R^{3a}$ ,  
 $(CH_2)_rNR^3C(O)NR^3R^{3a}$ ,  $(CH_2)_r-C(=NR^3)NR^3R^{3a}$ ,  
 $(CH_2)_rNR^3C(=NR^3)NR^3R^{3a}$ ,  $(CH_2)_rSO_2NR^3R^{3a}$ ,  
 $(CH_2)_rNR^3SO_2NR^3R^{3a}$ ,  $(CH_2)_rNR^3SO_2-C_{1-4}$  alkyl,  
 $(CH_2)_rNR^3SO_2CF_3$ ,  $(CH_2)_rNR^3SO_2$ -phenyl,  $(CH_2)_rS(O)_pCF_3$ ,  
10  $(CH_2)_rS(O)_p-C_{1-4}$  alkyl,  $(CH_2)_rS(O)_p$ -phenyl, and  
 $(CH_2)_r(CF_2)_rCF_3$ ;

$R^{4c}$ , at each occurrence, is selected from =O,  $(CR^3R^{3a})_rOR^2$ ,  
 $(CR^3R^{3a})_rF$ ,  $(CR^3R^{3a})_rBr$ ,  $(CR^3R^{3a})_rCl$ ,  $(CR^3R^{3a})_rCF_3$ ,  $C_{1-4}$   
15 alkyl,  $C_{2-6}$  alkenyl,  $C_{2-6}$  alkynyl,  $(CR^3R^{3a})_rCN$ ,  
 $(CR^3R^{3a})_rNO_2$ ,  $(CR^3R^{3a})_rNR^2R^{2a}$ ,  $(CR^3R^{3a})_rN(\rightarrow O)R^2R^{2a}$ ,  
 $(CR^3R^{3a})_rC(O)R^{2c}$ ,  $(CR^3R^{3a})_rNR^2C(O)R^{2b}$ ,  
 $(CR^3R^{3a})_rC(O)NR^2R^{2a}$ ,  $(CR^3R^{3a})_rN=CHOR^3$ ,  
 $(CR^3R^{3a})_rC(O)NR^2(CH_2)_2NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2C(O)NR^2R^{2a}$ ,  
20  $(CR^3R^{3a})_rC(=NR^2)NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2C(=NR^2)NR^2R^{2a}$ ,  
 $(CR^3R^{3a})_rSO_2NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2SO_2NR^2R^{2a}$ ,  
 $(CR^3R^{3a})_rC(O)NR^2SO_2-C_{1-4}$  alkyl,  $(CR^3R^{3a})_rNR^2SO_2R^{5a}$ ,  
 $(CR^3R^{3a})_rS(O)_pR^{5a}$ ,  $(CF_2)_rCF_3$ ,  $(CR^3R^{3a})_rC_{3-10}$  carbocycle  
substituted with 0-2  $R^{4b}$ , and  $(CR^3R^{3a})_r$  4-10 membered  
25 heterocycle substituted with 0-2  $R^{4b}$  and consisting of  
carbon atoms and from 1-4 heteroatoms selected from  
the group consisting of N, O, and  $S(O)_p$ ;

$R^5$ , at each occurrence, is selected from H,  $C_{1-6}$  alkyl, =O,  
30  $(CH_2)_rOR^3$ , F, Cl, Br, I, -CN,  $NO_2$ ,  $(CH_2)_rNR^3R^{3a}$ ,  
 $(CH_2)_rC(O)R^3$ ,  $(CH_2)_rC(O)OR^{3c}$ ,  $(CH_2)_rNR^3C(O)R^{3a}$ ,  
 $(CH_2)_rC(O)NR^3R^{3a}$ ,  $(CH_2)_rNR^3C(O)NR^3R^{3a}$ ,  $(CH_2)_rCH(=NOR^{3d})$ ,

$(\text{CH}_2)_r\text{C}(=\text{NR}^3)\text{NR}^3\text{R}^{3a}$ ,  $(\text{CH}_2)_r\text{NR}^3\text{C}(=\text{NR}^3)\text{NR}^3\text{R}^{3a}$ ,  
 $(\text{CH}_2)_r\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $(\text{CH}_2)_r\text{NR}^3\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $(\text{CH}_2)_r\text{NR}^3\text{SO}_2\text{-C}_{1-4}$   
 alkyl,  $(\text{CH}_2)_r\text{NR}^3\text{SO}_2\text{CF}_3$ ,  $(\text{CH}_2)_r\text{NR}^3\text{SO}_2\text{-phenyl}$ ,  
 $(\text{CH}_2)_r\text{S}(\text{O})_p\text{CF}_3$ ,  $(\text{CH}_2)_r\text{S}(\text{O})_p\text{-C}_{1-4}$  alkyl,  $(\text{CH}_2)_r\text{S}(\text{O})_p\text{-}$   
 5 phenyl,  $(\text{CF}_2)_r\text{CF}_3$ , phenyl substituted with 0-2  $\text{R}^6$ ,  
 naphthyl substituted with 0-2  $\text{R}^6$ , and benzyl  
 substituted with 0-2  $\text{R}^6$ ;

$\text{R}^{5a}$ , at each occurrence, is selected from  $\text{C}_{1-6}$  alkyl,  
 10  $(\text{CH}_2)_r\text{OR}^3$ ,  $(\text{CH}_2)_r\text{NR}^3\text{R}^{3a}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^3$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{OR}^{3c}$ ,  
 $(\text{CH}_2)_r\text{NR}^3\text{C}(\text{O})\text{R}^{3a}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{NR}^3\text{R}^{3a}$ ,  $(\text{CF}_2)_r\text{CF}_3$ , phenyl  
 substituted with 0-2  $\text{R}^6$ , naphthyl substituted with 0-2  
 $\text{R}^6$ , and benzyl substituted with 0-2  $\text{R}^6$ , provided that  
 $\text{R}^{5a}$  does not form a S-N or  $\text{S}(\text{O})_p\text{-C}(\text{O})$  bond;

15  $\text{R}^6$ , at each occurrence, is selected from H, OH,  $(\text{CH}_2)_r\text{OR}^2$ ,  
 halo,  $\text{C}_{1-4}$  alkyl, -CN,  $\text{NO}_2$ ,  $(\text{CH}_2)_r\text{NR}^2\text{R}^{2a}$ ,  $(\text{CH}_2)_r\text{C}(\text{O})\text{R}^{2b}$ ,  
 $\text{NR}^2\text{C}(\text{O})\text{R}^{2b}$ ,  $\text{NR}^2\text{C}(\text{O})\text{NR}^2\text{R}^{2a}$ ,  $\text{C}(=\text{NH})\text{NH}_2$ ,  $\text{NHC}(=\text{NH})\text{NH}_2$ ,  
 $\text{SO}_2\text{NR}^2\text{R}^{2a}$ ,  $\text{NR}^2\text{SO}_2\text{NR}^2\text{R}^{2a}$ , and  $\text{NR}^2\text{SO}_2\text{C}_{1-4}$  alkyl;

20  $\text{R}^7$ , at each occurrence, is selected from H, OH,  $\text{C}_{1-6}$  alkyl,  
 $\text{C}_{1-6}$  alkyl-C(O)-,  $\text{C}_{1-6}$  alkyl-O-,  $(\text{CH}_2)_n\text{-phenyl}$ ,  $\text{C}_{1-4}$   
 alkyl-OC(O)-,  $\text{C}_{6-10}$  aryl-O-,  $\text{C}_{6-10}$  aryl-OC(O)-,  $\text{C}_{6-10}$   
 aryl- $\text{CH}_2\text{-C}(\text{O})\text{-}$ ,  $\text{C}_{1-4}$  alkyl-C(O)O- $\text{C}_{1-4}$  alkyl-OC(O)-,  
 25  $\text{C}_{6-10}$  aryl-C(O)O- $\text{C}_{1-4}$  alkyl-OC(O)-,  
 $\text{C}_{1-6}$  alkyl-NH<sub>2</sub>-C(O)-, phenyl-NH<sub>2</sub>-C(O)-, and phenyl  $\text{C}_{1-4}$   
 alkyl-C(O)-;

30  $\text{R}^8$ , at each occurrence, is selected from H,  $\text{C}_{1-6}$  alkyl, and  
 $(\text{CH}_2)_n\text{-phenyl}$ ;

alternatively,  $\text{R}^7$  and  $\text{R}^8$ , when attached to the same  
 nitrogen, combine to form a 5-10 membered heterocyclic

ring consisting of carbon atoms and 0-2 additional heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

5 R<sup>9</sup>, at each occurrence, is selected from H, C<sub>1-6</sub> alkyl, and (CH<sub>2</sub>)<sub>n</sub>-phenyl;

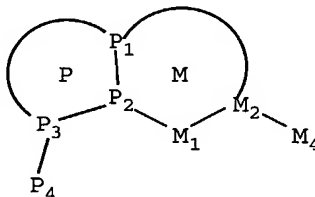
n, at each occurrence, is selected from 0, 1, 2, and 3;

10 p, at each occurrence, is selected from 0, 1, and 2;

r, at each occurrence, is selected from 0, 1, 2, 3, 4, 5, and 6; and,

15 t, at each occurrence, is selected from 0, 1, 2, and 3.

[2] In a preferred embodiment, the present invention provides a novel compound of Formula II:



20

II

or a stereoisomer or pharmaceutically acceptable salt thereof, wherein;

25 ring M, including P<sub>1</sub>, P<sub>2</sub>, M<sub>1</sub>, and M<sub>2</sub>, is a 5, 6, or 7 membered carbocycle or a 5, 6, or 7 membered heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)<sub>p</sub>, N, and NZ<sup>2</sup>;

30 ring M is substituted with 0-2 R<sup>1a</sup> and 0-2 carbonyl groups, and there are 0-3 ring double bonds;

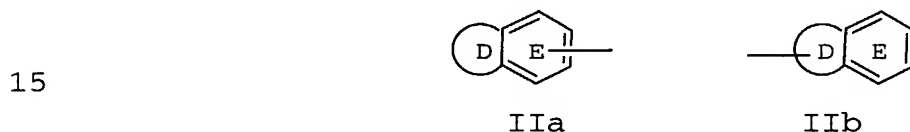
ring P, including P<sub>1</sub>, P<sub>2</sub>, and P<sub>3</sub>, is a 5 or 6 membered aromatic heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)<sub>p</sub>, and N;

5 alternatively, ring P, including P<sub>1</sub>, P<sub>2</sub>, and P<sub>3</sub>, is a 5 or 6 membered dihydro-aromatic heterocycle, consisting of: carbon atoms and 1-3 heteroatoms selected from O, S(O)<sub>p</sub>, and N;

10 ring P is substituted with 0-2 R<sup>1a</sup>;

one of P<sub>4</sub> and M<sub>4</sub> is -Z-A-B and the other -G<sub>1</sub>-G;

G is a group of formula IIa or IIb:



ring D, including the two atoms of Ring E to which it is attached, is a 5-6 membered ring consisting of carbon atoms and 0-2 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

20

ring D is substituted with 0-2 R and there are 0-3 ring double bonds;

25 E is selected from phenyl, pyridyl, pyrimidyl, pyrazinyl, and pyridazinyl, and is substituted with 1-3 R;

alternatively, ring D is absent, and ring E is selected from phenyl, pyridyl, pyrimidyl, and thienyl, and ring E is substituted with 1-3 R;

30

alternatively, ring D is absent, ring E is selected from phenyl, pyridyl, and thienyl, and ring E is substituted with 1 R and substituted with a 5-6

membered heterocycle consisting of: carbon atoms and  
 1-4 heteroatoms selected from the group consisting of  
 N, O, and S(O)<sub>p</sub>, wherein the 5-6 membered heterocycle  
 is substituted with 0-2 carbonyls and 1-3 R and there  
 5 are 0-3 ring double bonds;

R is selected from H, C<sub>1-4</sub> alkyl, F, Cl, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>,  
 OCH(CH<sub>3</sub>)<sub>2</sub>, CN, C(=NH)NH<sub>2</sub>, C(=NH)NHOH, C(=NH)NHOCH<sub>3</sub>,  
 NH<sub>2</sub>, NH(C<sub>1-3</sub> alkyl), N(C<sub>1-3</sub> alkyl)<sub>2</sub>, C(=NH)NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>,  
 10 CH<sub>2</sub>NH(C<sub>1-3</sub> alkyl), CH<sub>2</sub>N(C<sub>1-3</sub> alkyl)<sub>2</sub>, (CR<sup>8</sup>R<sup>9</sup>)<sub>t</sub>NR<sup>7</sup>R<sup>8</sup>,  
 C(O)NR<sup>7</sup>R<sup>8</sup>, CH<sub>2</sub>C(O)NR<sup>7</sup>R<sup>8</sup>, S(O)<sub>p</sub>NR<sup>7</sup>R<sup>8</sup>, CH<sub>2</sub>S(O)<sub>p</sub>NR<sup>7</sup>R<sup>8</sup>,  
 SO<sub>2</sub>R<sup>3</sup>, and OCF<sub>3</sub>;

alternatively, when 2 R groups are attached to adjacent  
 15 atoms, they combine to form methylenedioxy or  
 ethylenedioxy;

A is selected from:

C<sub>5-10</sub> carbocycle substituted with 0-2 R<sup>4</sup>, and  
 20 5-10 membered heterocycle substituted with 0-2 R<sup>4</sup> and  
 consisting of: carbon atoms and 1-4 heteroatoms selected  
 from the group consisting of N, O, and S(O)<sub>p</sub>;

X is selected from -(CR<sup>2</sup>R<sup>2a</sup>)<sub>1-4</sub>-, -C(O)-, -C(O)CR<sup>2</sup>R<sup>2a</sup>-,  
 25 -CR<sup>2</sup>R<sup>2a</sup>C(O)-, -S(O)<sub>2</sub>-, -S(O)<sub>2</sub>CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>S(O)<sub>2</sub>-,  
 -NR<sup>2</sup>S(O)<sub>2</sub>-, -S(O)<sub>2</sub>NR<sup>2</sup>-, -NR<sup>2</sup>C(O)-, -C(O)NR<sup>2</sup>-, NR<sup>2</sup>,  
 -NR<sup>2</sup>CR<sup>2</sup>R<sup>2a</sup>-, -CR<sup>2</sup>R<sup>2a</sup>NR<sup>2</sup>-, O, -OCR<sup>2</sup>R<sup>2a</sup>-, and -CR<sup>2</sup>R<sup>2a</sup>O-;

Y is a C<sub>3-7</sub> monocyclic carbocycle or 3-7 membered monocyclic  
 30 heterocycle, wherein the carbocycle or heterocycle  
 consists of: carbon atoms and 0-2 heteroatoms  
 selected from N, O, and S(O)<sub>p</sub>, the carbocycle or  
 heterocycle further comprises 0-2 double bonds and 0-2

carbonyl groups, and the carbocycle or heterocycle is substituted with 0-2  $R^4$ ;

alternatively, Y is  $CY^1Y^2$ , and  $Y^1$  and  $Y^2$  are independently  
5  $C_{1-3}$  alkyl substituted with 0-1  $R^4$ ;

Z is selected from a bond,  $CH_2$ ,  $CH_2CH_2$ ,  $CH_2O$ ,  $OCH_2$ ,  $C(O)$ ,  
NH,  $CH_2NH$ ,  $NHCH_2$ ,  $CH_2C(O)$ ,  $C(O)CH_2$ ,  $C(O)NH$ ,  $NHC(O)$ ,  
NHC(O) $CH_2C(O)NH$ ,  $S(O)_2$ ,  $CH_2S(O)_2$ ,  $S(O)_2(CH_2)$ ,  $SO_2NH$ ,  
10 and  $NHSO_2$ , provided that Z does not form a N-S,  $NCH_2N$ ,  
 $NCH_2O$ , or  $NCH_2S$  bond with either group to which it is  
attached;

$Z^2$  is selected from H,  $C_{1-4}$  alkyl, phenyl, benzyl,  $C(O)R^{3b}$ ,  
15  $S(O)R^{3f}$ , and  $S(O)_2R^{3f}$ ;

$R^{1a}$ , at each occurrence, is selected from H,  $-(CH_2)_r-R^{1b}$ ,  
 $-(CH(CH_3))_r-R^{1b}$ ,  $-(C(CH_3)_2)_r-R^{1b}$ ,  $-O-(CR^3R^{3a})_r-R^{1b}$ ,  
 $-NR^2-(CR^3R^{3a})_r-R^{1b}$ , and  $-S-(CR^3R^{3a})_r-R^{1b}$ , provided that  
20  $R^{1a}$  forms other than an N-halo, N-S, O-O, or N-CN bond;

alternatively, when two  $R^{1a}$  groups are attached to adjacent  
atoms or to the same carbon atom, together with the  
atoms to which they are attached, they form a 5-7  
25 membered ring consisting of: carbon atoms and 0-2  
heteroatoms selected from the group consisting of N,  
O, and  $S(O)_p$ , this ring being substituted with 0-2  $R^{4b}$   
and comprising: 0-3 double ring bonds;

30  $R^{1b}$  is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , F,  
Cl, Br, I, -CN, -CHO,  $CF_3$ ,  $OR^2$ ,  $NR^2R^{2a}$ ,  $C(O)R^{2b}$ ,  $CO_2R^{2b}$ ,  
 $OC(O)R^2$ ,  $CO_2R^{2a}$ ,  $S(O)_pR^{2b}$ ,  $NR^2(CH_2)_rOR^2$ ,  $NR^2C(O)R^{2b}$ ,  
 $NR^2C(O)NHR^2$ ,  $NR^2C(O)_2R^{2a}$ ,  $OC(O)NR^2R^{2a}$ ,  $C(O)NR^2R^{2a}$ ,



C(O)NR<sup>2</sup>(CH<sub>2</sub>)<sub>r</sub>OR<sup>2</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>R<sup>2</sup>, C<sub>5-6</sub> carbocycle substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of carbon atoms and from 1-4 heteroatoms selected from the group  
 5 consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>1b</sup> forms other than an O-O, N-halo, N-S, or N-CN bond and provided that S(O)<sub>p</sub>R<sup>2</sup> forms other than S(O)<sub>2</sub>H or S(O)H;

R<sup>2</sup>, at each occurrence, is selected from H, CF<sub>3</sub>, CH<sub>3</sub>,  
 10 CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, C(CH<sub>3</sub>)<sub>3</sub>, benzyl, C<sub>5-6</sub> carbocycle substituted with 0-2 R<sup>4b</sup>, a C<sub>5-6</sub> carbocycle-CH<sub>2</sub>- substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of: carbon  
 15 atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2a</sup>, at each occurrence, is selected from H, CF<sub>3</sub>, CH<sub>3</sub>,  
 CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>,  
 20 CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, C(CH<sub>3</sub>)<sub>3</sub>, benzyl, C<sub>5-6</sub> carbocycle substituted with 0-2 R<sup>4b</sup>, and 5-6 membered heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

25 alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R<sup>4b</sup> and consisting of: 0-1  
 30 additional heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2b</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>,

CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, C(CH<sub>3</sub>)<sub>3</sub>, benzyl, C<sub>5-6</sub>  
carbocycle substituted with 0-2 R<sup>4b</sup>, and 5-6 membered  
heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of:  
carbon atoms and 1-4 heteroatoms selected from the  
5 group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2c</sup>, at each occurrence, is selected from CF<sub>3</sub>, OH, C<sub>1-4</sub>  
alkoxy, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>,  
CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, C(CH<sub>3</sub>)<sub>3</sub>, benzyl, C<sub>5-6</sub>  
10 carbocycle substituted with 0-2 R<sup>4b</sup>, and 5-6 membered  
heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of  
carbon atoms and from 1-4 heteroatoms selected from  
the group consisting of N, O, and S(O)<sub>p</sub>;

15 R<sup>2d</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl  
substituted with 0-2 R<sup>4c</sup>, -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-C<sub>3-6</sub> carbocycle  
substituted with 0-2 R<sup>4c</sup>, and -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-5-6 membered  
heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of:  
carbon atoms and 1-4 heteroatoms selected from the  
20 group consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2d</sup>  
forms other than a N-halo, N-C-halo, S(O)<sub>p</sub>-halo, O-  
halo, N-S, S-N, S(O)<sub>p</sub>-S(O)<sub>p</sub>, S-O, O-N, O-S, or O-O  
moiety;

25 alternatively, when two R<sup>2d</sup>'s are attached to the same  
nitrogen atom, then R<sup>2d</sup> and R<sup>2d</sup>, together with the  
nitrogen atom to which they are attached, combine to  
form a 5 or 6 membered saturated, partially saturated  
or unsaturated ring substituted with 0-2 R<sup>4b</sup> and  
30 consisting of: 0-1 additional heteroatoms selected  
from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2e</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl  
substituted with 0-2 R<sup>4c</sup>, -(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub>-C<sub>3-6</sub> carbocycle

substituted with 0-2  $R^{4c}$ , and  $-(CR^3R^{3a})_r$ -5-6 membered heterocycle substituted with 0-2  $R^{4c}$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ , provided that  $R^{2e}$   
5 forms other than a  $C(O)$ -halo or  $C(O)$ - $S(O)_p$  moiety;

$R^3$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , benzyl, and phenyl;

10  $R^{3a}$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , benzyl, and phenyl;

alternatively,  $R^3$  and  $R^{3a}$ , together with the nitrogen atom to which they are attached, combine to form a 5 or 6  
15 membered saturated, partially unsaturated, or unsaturated ring consisting of: carbon atoms and the nitrogen atom to which  $R^3$  and  $R^{3a}$  are attached;

$R^{3c}$ , at each occurrence, is selected from  $CH_3$ ,  $CH_2CH_3$ ,  
20  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , benzyl, and phenyl;

$R^{3d}$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH_2$ -phenyl,  $CH_2CH_2$ -phenyl, and  $C(=O)R^{3c}$ ;  
25

$R^{3g}$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , cyclopropyl, cyclopropyl-methyl, benzyl, and phenyl;

30 alternatively, when  $R^3$  and  $R^{3g}$  are attached to the same carbon atom, they combine with the attached carbon atom to form a cyclopropyl group;

- $R^4$ , at each occurrence, is selected from H, =O,  $OR^2$ ,  $CH_2OR^2$ ,  $(CH_2)_2OR^2$ , F, Cl, Br, I,  $C_{1-4}$  alkyl, -CN,  $NO_2$ ,  $NR^2R^{2a}$ ,  $CH_2NR^2R^{2a}$ ,  $(CH_2)_2NR^2R^{2a}$ ,  $C(O)R^{2c}$ ,  $NR^2C(O)R^{2b}$ ,  $C(O)NR^2R^{2a}$ ,  $SO_2NR^2R^{2a}$ ,  $S(O)_pR^{5a}$ ,  $CF_3$ ,  $CF_2CF_3$ , 5-6 membered carbocycle substituted with 0-1  $R^5$ , and a 5-6 membered heterocycle substituted with 0-1  $R^5$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;
- $R^{4b}$ , at each occurrence, is selected from H, =O,  $OR^3$ ,  $CH_2OR^3$ , F, Cl,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH_2CH_2CH_2CH_3$ ,  $CH_2CH(CH_3)_2$ ,  $CH(CH_3)CH_2CH_3$ ,  $C(CH_3)_3$ , -CN,  $NO_2$ ,  $NR^3R^{3a}$ ,  $CH_2NR^3R^{3a}$ ,  $C(O)R^3$ ,  $CH_2-C(O)R^3$ ,  $C(O)OR^{3c}$ ,  $CH_2C(O)OR^{3c}$ ,  $NR^3C(O)R^{3a}$ ,  $CH_2NR^3C(O)R^{3a}$ ,  $C(O)NR^3R^{3a}$ ,  $CH_2C(O)NR^3R^{3a}$ ,  $NR^3C(O)NR^3R^{3a}$ ,  $CH_2NR^3C(O)NR^3R^{3a}$ ,  $C(=NR^3)NR^3R^{3a}$ ,  $CH_2C(=NR^3)NR^3R^{3a}$ ,  $NR^3C(=NR^3)NR^3R^{3a}$ ,  $CH_2NR^3C(=NR^3)NR^3R^{3a}$ ,  $SO_2NR^3R^{3a}$ ,  $CH_2SO_2NR^3R^{3a}$ ,  $NR^3SO_2NR^3R^{3a}$ ,  $CH_2NR^3SO_2NR^3R^{3a}$ ,  $NR^3SO_2-C_{1-4}$  alkyl,  $CH_2NR^3SO_2-C_{1-4}$  alkyl,  $NR^3SO_2CF_3$ ,  $CH_2NR^3SO_2CF_3$ ,  $NR^3SO_2$ -phenyl,  $CH_2NR^3SO_2$ -phenyl,  $S(O)_pCF_3$ ,  $CH_2S(O)_pCF_3$ ,  $S(O)_p-C_{1-4}$  alkyl,  $CH_2S(O)_p-C_{1-4}$  alkyl,  $S(O)_p$ -phenyl,  $CH_2S(O)_p$ -phenyl,  $CF_3$ , and  $CH_2-CF_3$ ;
- $R^{4c}$ , at each occurrence, is selected from =O,  $(CR^3R^{3a})_rOR^2$ ,  $(CR^3R^{3a})_rF$ ,  $(CR^3R^{3a})_rBr$ ,  $(CR^3R^{3a})_rCl$ ,  $(CR^3R^{3a})_rCF_3$ ,  $C_{1-4}$  alkyl,  $C_{2-4}$  alkenyl,  $C_{2-4}$  alkynyl,  $(CR^3R^{3a})_rCN$ ,  $(CR^3R^{3a})_rNO_2$ ,  $(CR^3R^{3a})_rNR^2R^{2a}$ ,  $(CR^3R^{3a})_rN(\rightarrow O)R^2R^{2a}$ ,  $(CR^3R^{3a})_rC(O)R^{2c}$ ,  $(CR^3R^{3a})_rNR^2C(O)R^{2b}$ ,  $(CR^3R^{3a})_rC(O)NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2C(O)NR^2R^{2a}$ ,  $(CR^3R^{3a})_rSO_2NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2SO_2NR^2R^{2a}$ ,  $(CR^3R^{3a})_rNR^2SO_2R^{5a}$ ,  $(CR^3R^{3a})_rS(O)_pR^{5a}$ ,  $(CF_2)_rCF_3$ ,  $(CR^3R^{3a})_rC_{3-10}$  carbocycle substituted with 0-2  $R^{4b}$ , and

(CR<sup>3</sup>R<sup>3a</sup>)<sub>r</sub> 5-10 membered heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

5

R<sup>5</sup>, at each occurrence, is selected from H, =O, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, C(CH<sub>3</sub>)<sub>3</sub>, OR<sup>3</sup>, CH<sub>2</sub>OR<sup>3</sup>, F, Cl, -CN, NO<sub>2</sub>, NR<sup>3</sup>R<sup>3a</sup>, CH<sub>2</sub>NR<sup>3</sup>R<sup>3a</sup>, C(O)R<sup>3</sup>, CH<sub>2</sub>C(O)R<sup>3</sup>, C(O)OR<sup>3c</sup>, CH<sub>2</sub>C(O)OR<sup>3c</sup>, NR<sup>3</sup>C(O)R<sup>3a</sup>, C(O)NR<sup>3</sup>R<sup>3a</sup>, NR<sup>3</sup>C(O)NR<sup>3</sup>R<sup>3a</sup>, CH(=NOR<sup>3d</sup>), C(=NR<sup>3</sup>)NR<sup>3</sup>R<sup>3a</sup>, NR<sup>3</sup>C(=NR<sup>3</sup>)NR<sup>3</sup>R<sup>3a</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>3a</sup>, NR<sup>3</sup>SO<sub>2</sub>NR<sup>3</sup>R<sup>3a</sup>, NR<sup>3</sup>SO<sub>2</sub>-C<sub>1-4</sub> alkyl, NR<sup>3</sup>SO<sub>2</sub>CF<sub>3</sub>, NR<sup>3</sup>SO<sub>2</sub>-phenyl, S(O)<sub>p</sub>CF<sub>3</sub>, S(O)<sub>p</sub>-C<sub>1-4</sub> alkyl, S(O)<sub>p</sub>-phenyl, CF<sub>3</sub>, phenyl substituted with 0-2 R<sup>6</sup>, naphthyl substituted with 0-2 R<sup>6</sup>, and benzyl substituted with 0-2 R<sup>6</sup>;

10

15

R<sup>6</sup>, at each occurrence, is selected from H, OH, OR<sup>2</sup>, F, Cl, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, C(CH<sub>3</sub>)<sub>3</sub>, -CN, NO<sub>2</sub>, NR<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2b</sup>, CH<sub>2</sub>C(O)R<sup>2b</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, NR<sup>2</sup>C(O)NR<sup>2</sup>R<sup>2a</sup>, C(=NH)NH<sub>2</sub>, NHC(=NH)NH<sub>2</sub>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, and NR<sup>2</sup>SO<sub>2</sub>C<sub>1-4</sub> alkyl; and,

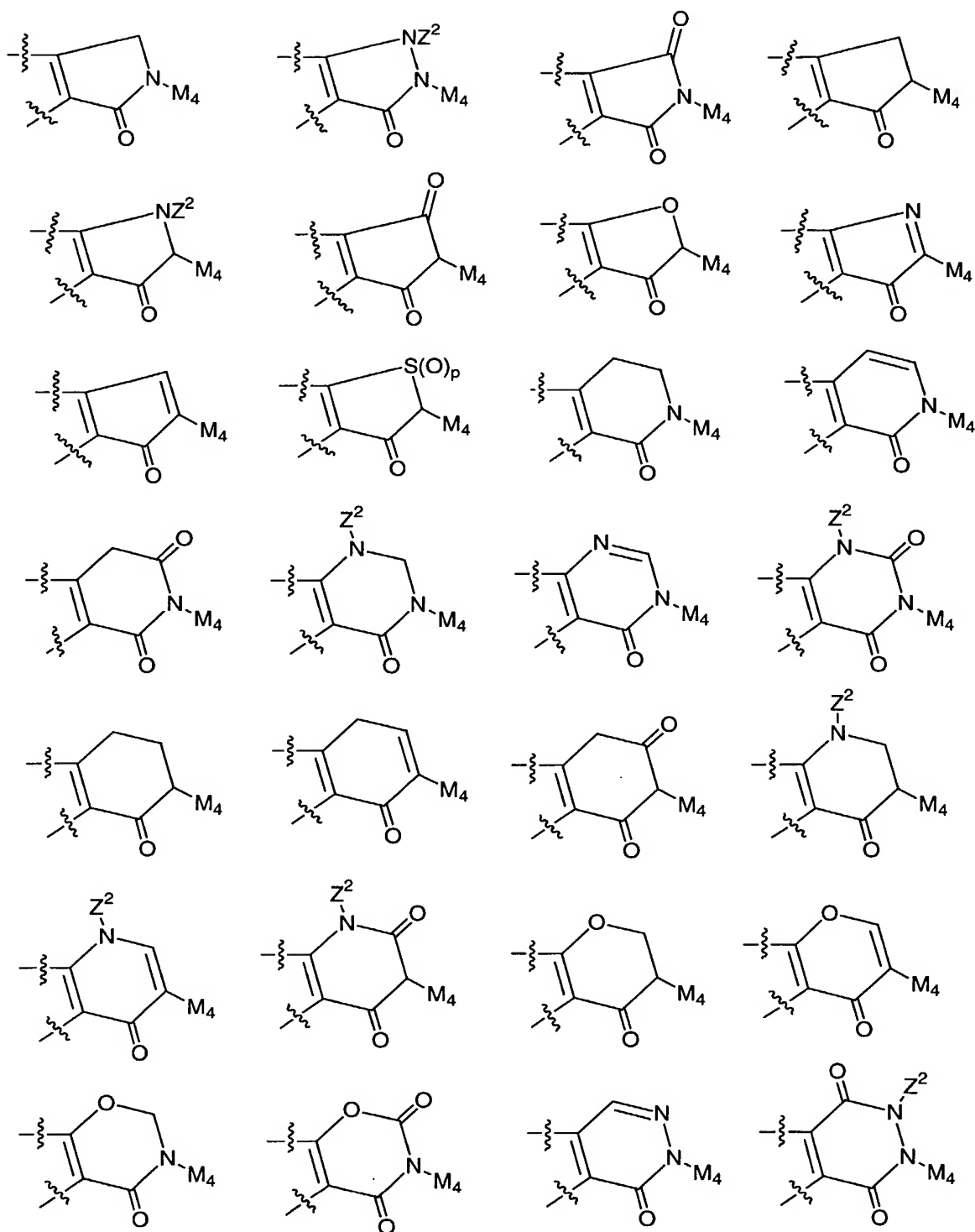
20

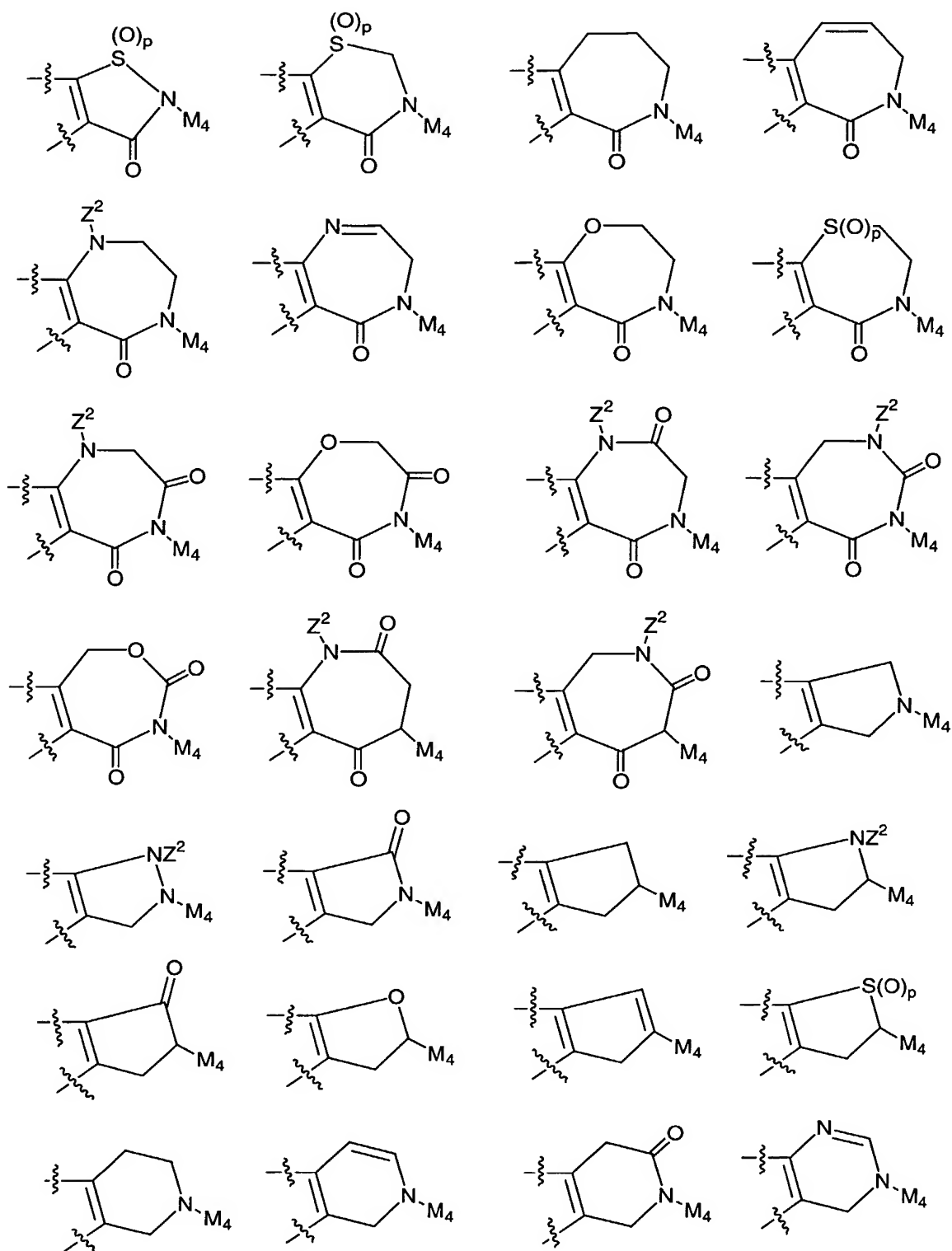
r, at each occurrence, is selected from 0, 1, 2, and 3.

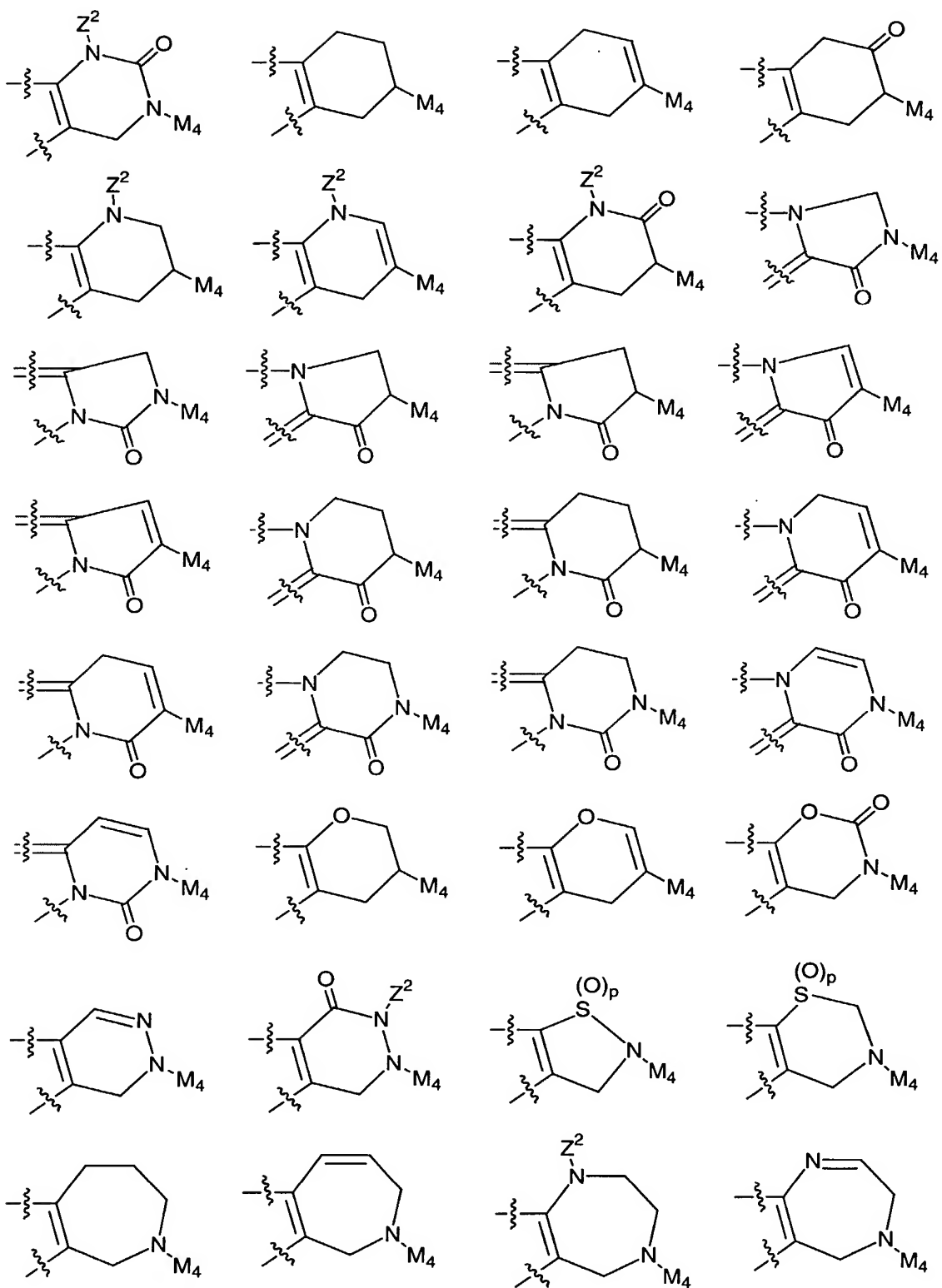
25

[3] In another preferred embodiment, the present invention provides a novel compound, wherein:

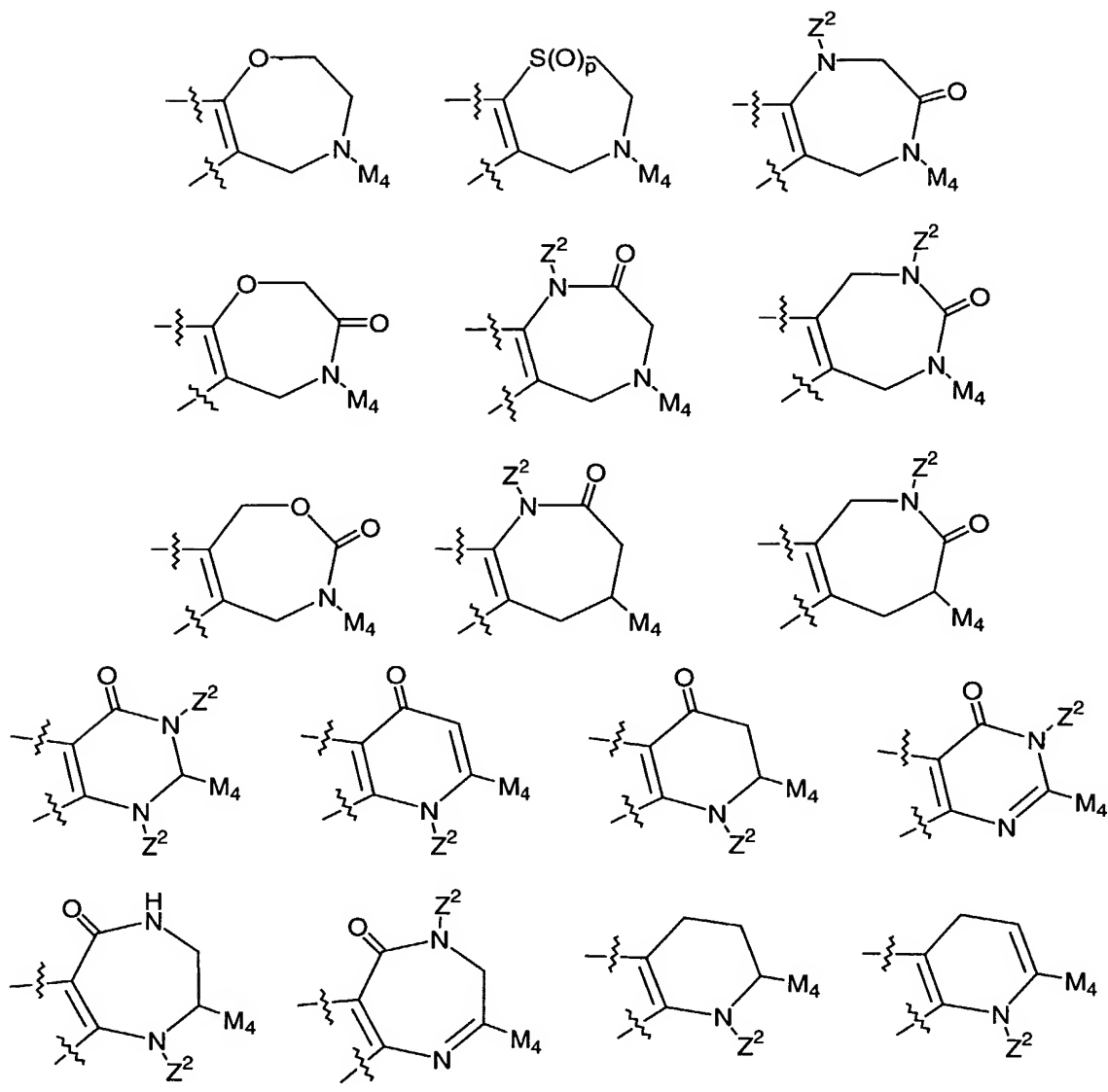
30 ring M is substituted with 0-2 R<sup>1a</sup> and is selected from the group:



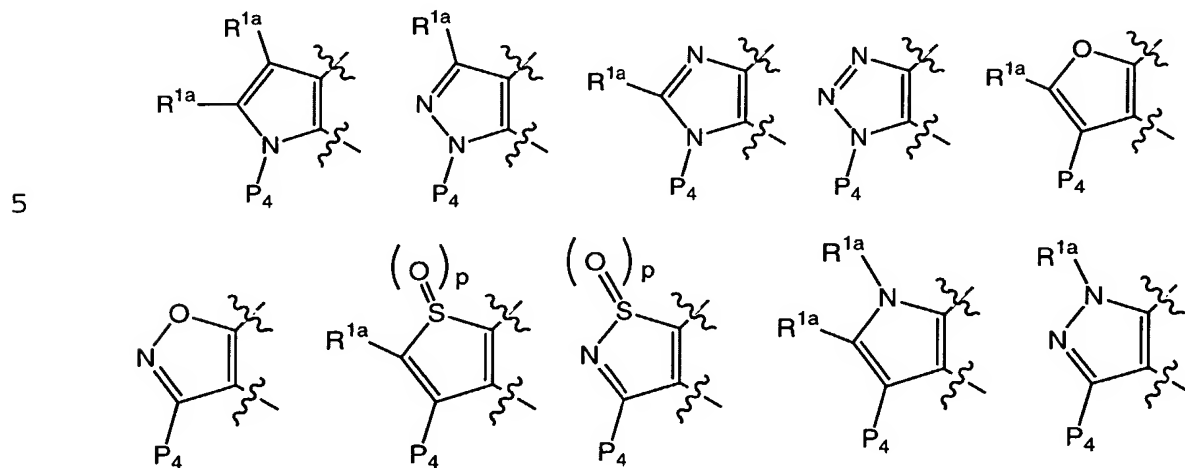


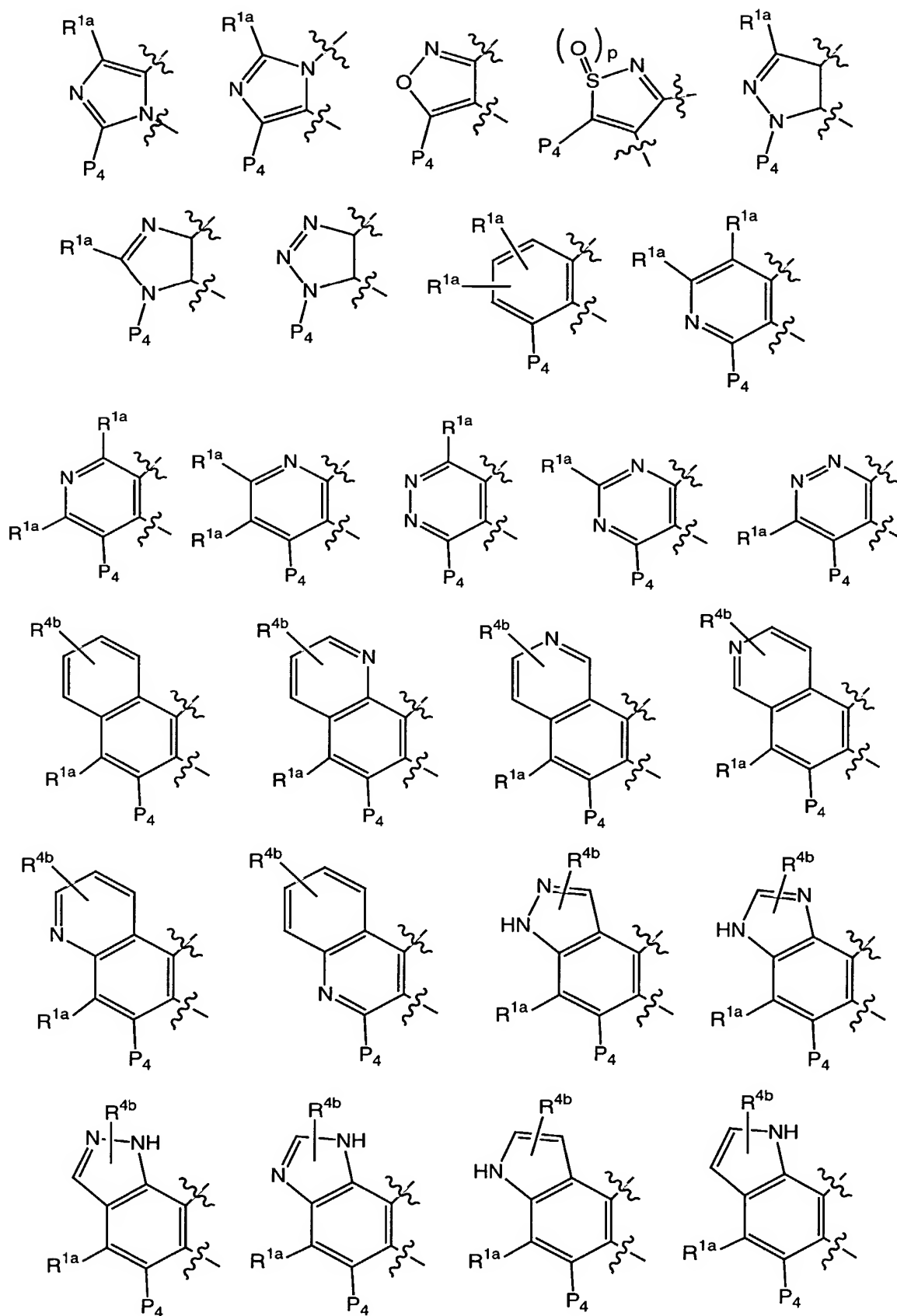


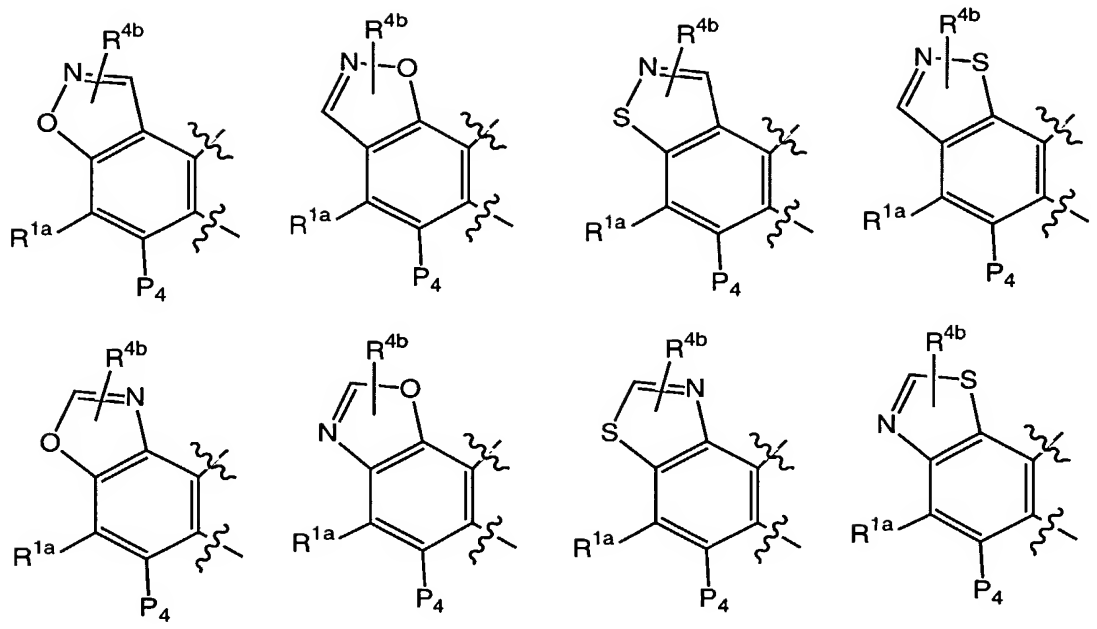




ring P, including P<sub>1</sub>, P<sub>2</sub>, P<sub>3</sub>, and P<sub>4</sub> is selected from group:



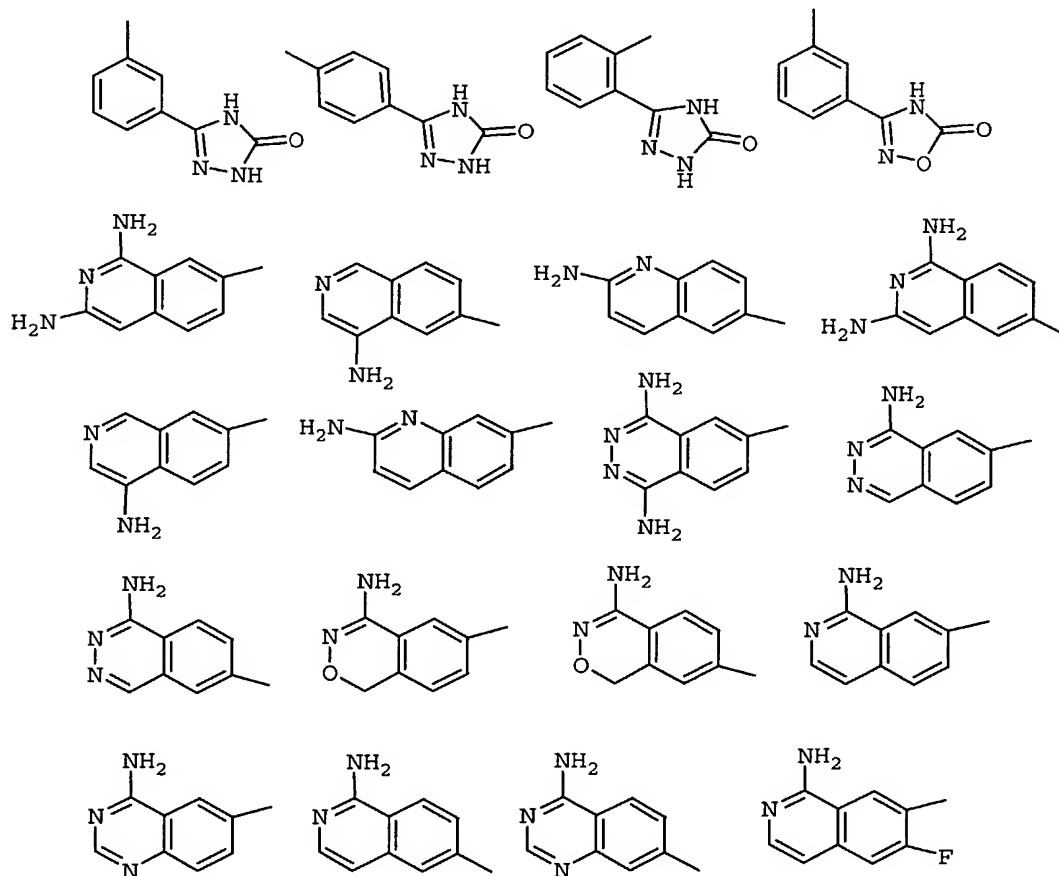


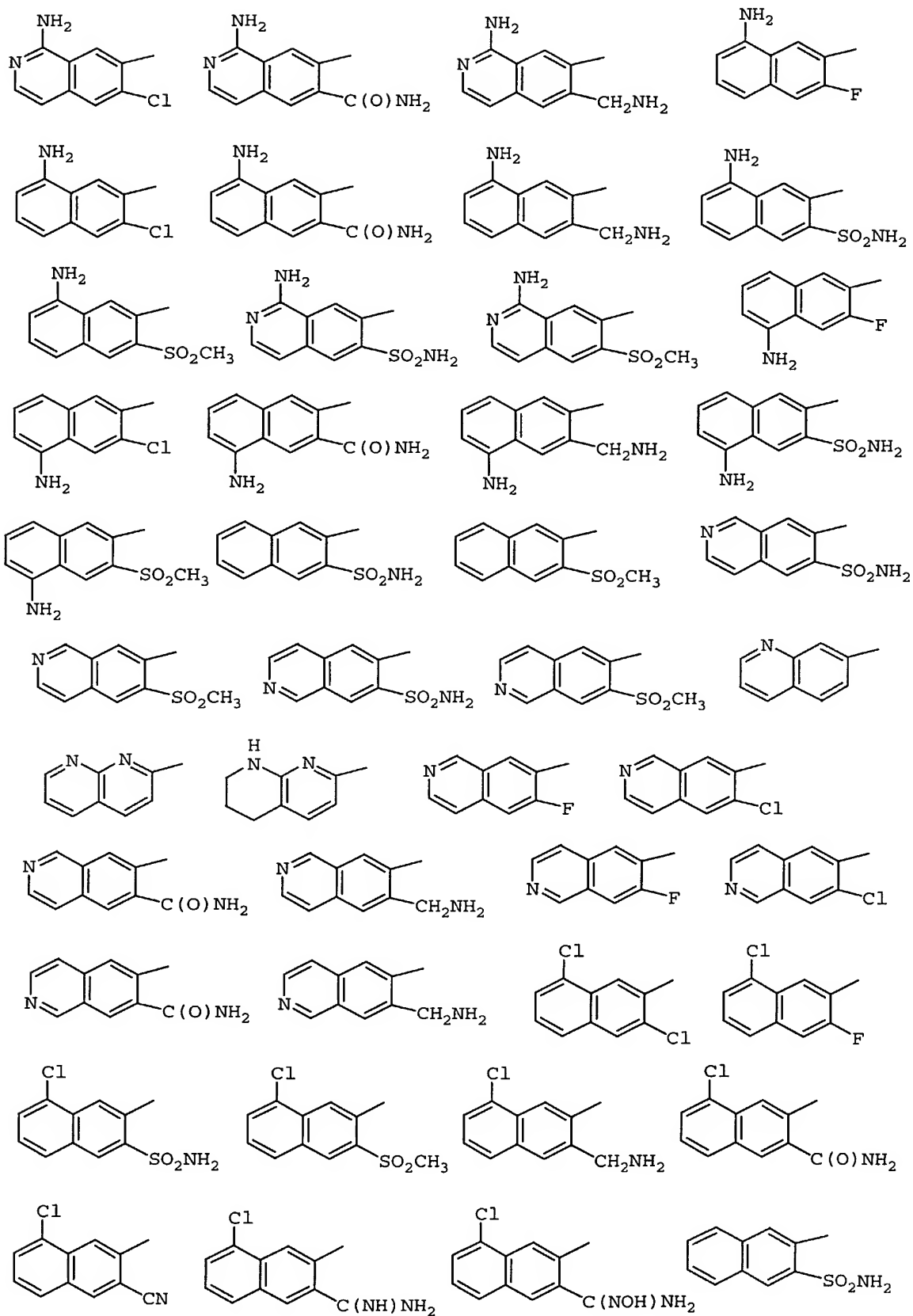


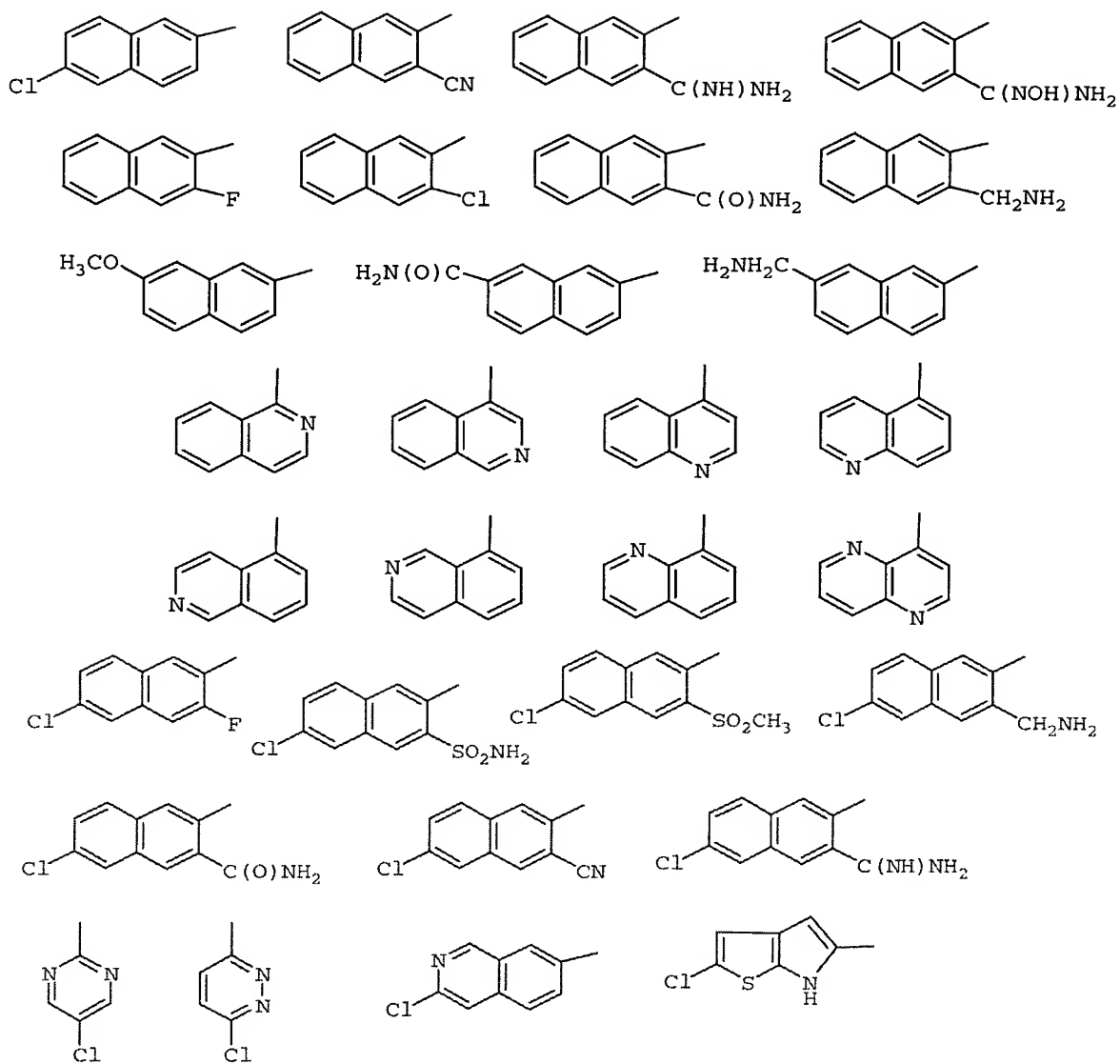
G is selected from the group:

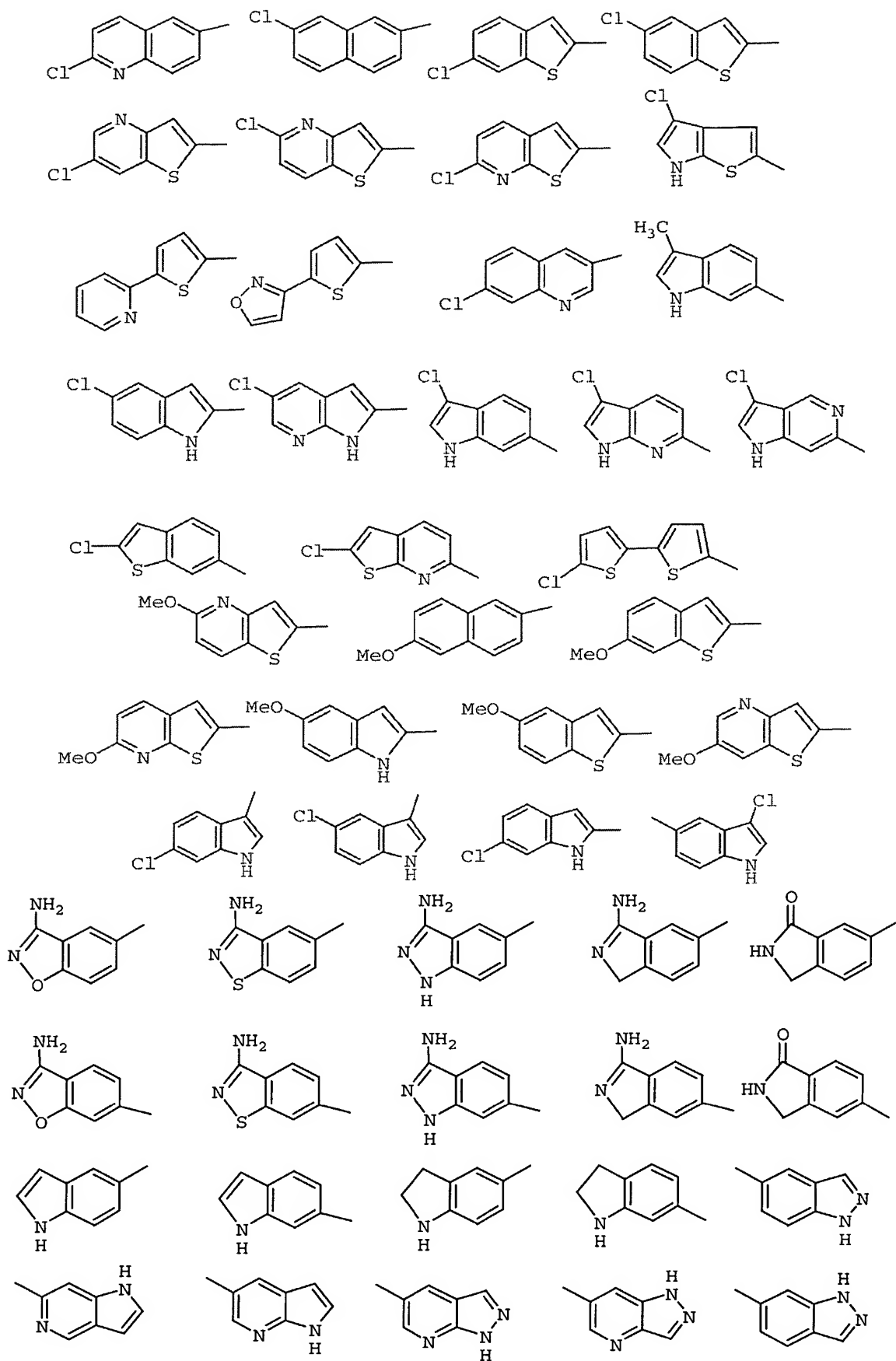
- phenyl; 2,5-bis-aminomethyl-phenyl;
- 5 2-amido-4-methoxy-phenyl; 2-amido-5-chloro-phenyl;
- 2-amido-phenyl; 2-aminomethyl-3-fluoro-phenyl;
- 2-aminomethyl-3-methoxy-phenyl;
- 2-aminomethyl-4-fluoro-phenyl;
- 2-aminomethyl-4-methoxy-phenyl;
- 10 2-aminomethyl-5-fluoro-phenyl;
- 2-aminomethyl-5-methoxy-phenyl;
- 2-aminomethyl-6-fluoro-phenyl; 2-aminomethyl-phenyl;
- 2-amino-pyrid-4-yl; 2-aminosulfonyl-4-methoxy-phenyl;
- 2-aminosulfonyl-phenyl; 2-aminomethyl-4-ethyl-phenyl; 2-
- 15 aminosulfonyl-4-ethyl-phenyl; 2-amido-4-ethyl-phenyl;
- 2-hydroxy-4-methoxy-phenyl; 2-methylsulfonyl-phenyl;
- 3-(N,N-dimethylamino)-4-chloro-phenyl;
- 3-(N,N-dimethylamino)-phenyl; 3-(N-hydroxy-amidino)-phenyl;
- 3-(N-methoxy-amidino)-phenyl;
- 20 3-(N-methylamino)-4-chloro-phenyl;
- 3-(N-methylamino)-phenyl; 3-amidino-phenyl;
- 3-amido-6-hydroxy-phenyl; 3-amido-phenyl;
- 3-amino-4-chloro-phenyl; 3-aminomethyl-phenyl;
- 3-amino-phenyl; 3-chloro-4-fluoro-phenyl; 3-chloro-phenyl;

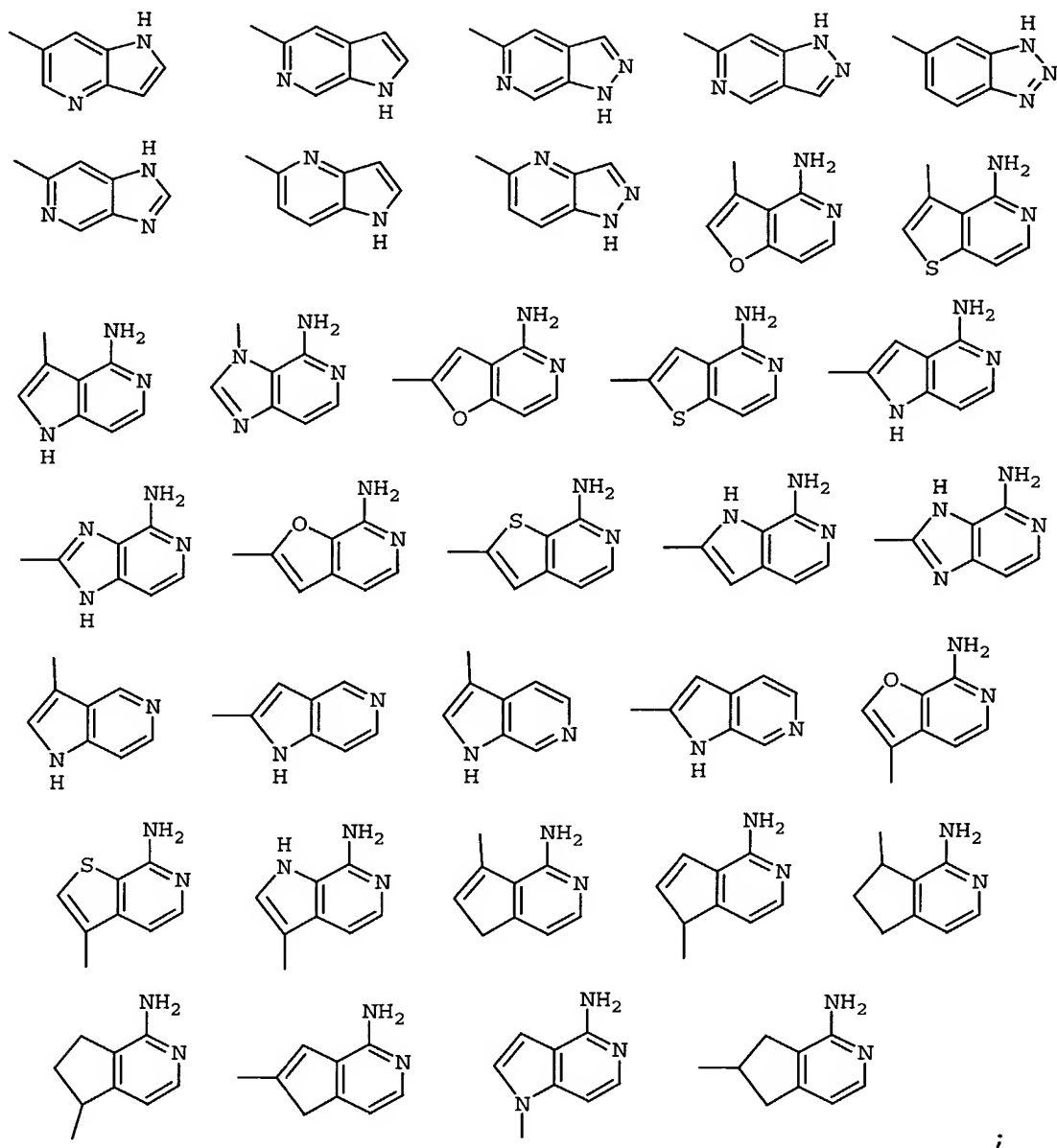
- 3-hydroxy-4-methoxy-phenyl;  
 4-(N,N-dimethylamino)-5-chloro-thien-2-yl;  
 4-(N-methylamino)-5-chloro-thien-2-yl;  
 4-amino-5-chloro-thien-2-yl; 4-amino-pyrid-2-yl;  
 5 4-chloro-3-fluoro-phenyl; 4-chloro-phenyl;  
 4-chloro-pyrid-2-yl; 4-ethyl-phenyl; 4-ethyl-2-methylsulfonyl-phenyl;  
 4-ethyl-2-methoxy-phenyl;  
 4-methoxy-2-methylsulfonyl-phenyl; 4-methoxy-phenyl;  
 2-methoxy-pyrid-5-yl;  
 10 5-(N,N-dimethylamino)-4-chloro-thien-2-yl;  
 5-(N-methylamino)-4-chloro-thien-2-yl;  
 5-amino-4-chloro-thien-2-yl;  
 5-chloro-2-aminosulfonyl-phenyl;  
 5-chloro-2-methylsulfonyl-phenyl; 5-chloro-pyrid-2-yl;  
 15 5-chloro-thien-2-yl; 5-methoxy-thien-2-yl;  
 5-methyl-thien-2-yl; 5-fluoro-thien-2-yl;  
 6-amino-5-chloro-pyrid-2-yl; 6-amino-pyrid-2-yl;











- 5  $G_1$  is absent or is selected from  $(CR^3R^{3a})_{1-3}$ ,  $CR^3=CR^3$ ,  
 $(CR^3R^{3a})_u C(O)(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_u O(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_u NR^{3b}(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_u C(O)NR^{3b}(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_u NR^{3b}C(O)(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_u NR^{3b}C(O)(CR^3R^{3a})_u C(O)NR^{3b}(CR^3R^{3a})_w$ ,  
10  $(CR^3R^{3a})_u S(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_u S(O)(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_u S(O)_2(CR^3R^{3a})_w$ ,  $(CR^3R^{3a})_u S(O)NR^{3b}(CR^3R^{3a})_w$ ,  
 $(CR^3R^{3a})_u NR^{3b}S(O)_2(CR^3R^{3a})_w$ , and  
 $(CR^3R^{3a})_u S(O)_2NR^{3b}(CR^3R^{3a})_w$ , wherein  $u + w$  total 0, 1,



or 2, provided that  $G_1$  does not form a N-S,  $NCH_2N$ ,  $NCH_2O$ , or  $NCH_2S$  bond with either group to which it is attached;

5 A is selected from one of the following carbocycles and heterocycles which are substituted with 0-2  $R^4$ ;

cyclohexyl, phenyl, piperidinyl, piperazinyl, pyridyl, pyrimidyl, furanyl, morpholinyl, thienyl, pyrrolyl, pyrrolidinyl, oxazolyl, isoxazolyl, 10 thiazolyl, isothiazolyl, pyrazolyl, imidazolyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazolyl, 1,2,5-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,2,5-thiadiazolyl, 1,3,4-thiadiazolyl, 15 1,2,3-triazolyl, 1,2,4-triazolyl, 1,2,5-triazolyl, 1,3,4-triazolyl, benzofuranyl, benzothiofuranyl, indolyl, indolyl, benzimidazolyl, benzoxazolyl, benzthiazolyl, indazolyl, benzisoxazolyl, benzisothiazolyl, and isoindazolyl;

20

X is selected from  $-(CR^2R^{2a})_{1-2}-$ ,  $-C(O)-$ ,  $-S(O)_2-$ ,  $-NR^2S(O)_2-$ ,  $-NR^2S(O)_2NR^2-$ ,  $-NR^2C(O)-$ ,  $-C(O)NR^2-$ ,  $NR^2$ ,  $-NR^2CR^2R^{2a}-$ ,  $-CR^2R^{2a}NR^2-$ , O,  $-OCR^2R^{2a}-$ , and  $-CR^2R^{2a}O-$ ;

25 Y is a  $C_{3-6}$  monocyclic carbocycle or 5-6 membered monocyclic heterocycle, wherein the carbocycle or heterocycle consists of carbon atoms and 0-2 heteroatoms selected from N, O, and S(O)<sub>p</sub>, the carbocycle or heterocycle further comprises 0-1 double bonds and 0-1 carbonyl 30 groups, and the carbocycle or heterocycle is substituted with 0-2  $R^4$ ;

alternatively, Y is  $CY^1Y^2$ , and  $Y^1$  and  $Y^2$  are independently  $C_{1-2}$  alkyl substituted with 0-1  $R^4$ ;

35

$R^{1a}$ , at each occurrence, is selected from H,  $R^{1b}$ ,  
 $CH(CH_3)R^{1b}$ ,  $C(CH_3)_2R^{1b}$ ,  $CH_2R^{1b}$ , and  $CH_2CH_2R^{1b}$ , provided  
that  $R^{1a}$  forms other than an N-halo, N-S, or N-CN bond;

5 alternatively, when two  $R^{1a}$  groups are attached to adjacent  
atoms or to the same carbon atom, together with the  
atoms to which they are attached they form a 5-6  
membered ring consisting of: carbon atoms and 0-2  
heteroatoms selected from the group consisting of N,  
10 O, and  $S(O)_p$ , this ring being substituted with 0-2  $R^{4b}$   
and 0-3 ring double bonds;

$R^{1b}$  is selected from H,  $CH_3$ ,  $CH_2CH_3$ , F, Cl, Br, -CN, -CHO,  
 $CF_3$ ,  $OR^2$ ,  $NR^2R^{2a}$ ,  $C(O)R^{2b}$ ,  $CO_2R^{2b}$ ,  $OC(O)R^2$ ,  $CO_2R^{2a}$ ,  
15  $S(O)_pR^2$ ,  $NR^2(CH_2)_rOR^2$ ,  $NR^2C(O)R^{2b}$ ,  $C(O)NR^2R^{2a}$ ,  $SO_2NR^2R^{2a}$ ,  
 $NR^2SO_2R^2$ , phenyl substituted with 0-2  $R^{4b}$ , and 5-6  
membered aromatic heterocycle consisting of carbon  
atoms and from 1-4 heteroatoms selected from the group  
consisting of N, O, and  $S(O)_p$  and substituted with 0-2  
20  $R^{4b}$ , provided that  $R^{1b}$  forms other than an O-O, N-halo,  
N-S, or N-CN bond;

$R^2$ , at each occurrence, is selected from H,  $CF_3$ ,  $CH_3$ ,  
 $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , phenyl substituted with  
25 0-2  $R^{4b}$ , benzyl substituted with 0-2  $R^{4b}$ , and 5-6  
membered aromatic heterocycle substituted with 0-2  $R^{4b}$   
and consisting of: carbon atoms and 1-4 heteroatoms  
selected from the group consisting of N, O, and  $S(O)_p$ ;

30  $R^{2a}$ , at each occurrence, is selected from H,  $CF_3$ ,  $CH_3$ ,  
 $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , benzyl, phenyl substituted  
with 0-2  $R^{4b}$ , and 5-6 membered aromatic heterocycle  
substituted with 0-2  $R^{4b}$  and consisting of: carbon

atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-2 R<sup>4b</sup> and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2b</sup>, at each occurrence, is selected from CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, benzyl, phenyl substituted with 0-2 R<sup>4b</sup>, and 5-6 membered aromatic heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2c</sup>, at each occurrence, is selected from CF<sub>3</sub>, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, benzyl, phenyl substituted with 0-2 R<sup>4b</sup>, and 5-6 membered aromatic heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2d</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl substituted with 0-2 R<sup>4c</sup>, C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, -(CR<sup>3</sup>R<sup>3a</sup>)-C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, 5-6 membered heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and -(CR<sup>3</sup>R<sup>3a</sup>)-5-6 membered heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group

consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2d</sup> forms other than a N-halo, N-C-halo, S(O)<sub>p</sub>-halo, O-halo, N-S, S-N, S(O)<sub>p</sub>-S(O)<sub>p</sub>, S-O, O-N, O-S, or O-O moiety;

5 R<sup>2e</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl substituted with 0-2 R<sup>4c</sup>, C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, -(CR<sup>3</sup>R<sup>3a</sup>)-C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, 5-6 membered heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of: carbon atoms and 1-4  
 10 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and -(CR<sup>3</sup>R<sup>3a</sup>)-5-6 membered heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2e</sup> forms  
 15 other than a C(O)-halo or C(O)-S(O)<sub>p</sub> moiety;

R<sup>4</sup>, at each occurrence, is selected from H, (CH<sub>2</sub>)<sub>2</sub>OR<sup>2</sup>, CH<sub>2</sub>OR<sup>2</sup>, OR<sup>2</sup>, F, Cl, Br, I, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>,  
 20 C(CH<sub>3</sub>)<sub>3</sub>, -CN, NO<sub>2</sub>, NR<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, CF<sub>3</sub>, and CF<sub>2</sub>CF<sub>3</sub>;

R<sup>4a</sup> is selected from -(CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-5-6 membered carbocycle  
 25 substituted with 0-3 R<sup>4c</sup>, -(CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-5-6 membered heterocycle substituted with 0-3 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>NR<sup>2d</sup>R<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>N(→O)R<sup>2d</sup>R<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>OR<sup>2d</sup>,  
 30 (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-NR<sup>2d</sup>C(O)R<sup>2e</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-C(O)R<sup>2e</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-OC(O)R<sup>2e</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-C(O)NR<sup>2d</sup>R<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-C(O)OR<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-NR<sup>2d</sup>C(O)NR<sup>2d</sup>R<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-NR<sup>2d</sup>C(O)OR<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-SO<sub>2</sub>NR<sup>2d</sup>R<sup>2d</sup>,

$(\text{CR}^3\text{R}^{3g})_r\text{-NR}^{2d}\text{SO}_2\text{R}^{2d}$ , and  $(\text{CR}^3\text{R}^{3g})_r\text{-S(O)}_p\text{R}^{2d}$ , provided that  $\text{S(O)}_p\text{R}^{2d}$  forms other than  $\text{S(O)}_2\text{H}$  or  $\text{S(O)H}$ ;

$\text{R}^{4b}$ , at each occurrence, is selected from H, =O,  $\text{OR}^3$ ,  
 5  $\text{CH}_2\text{OR}^3$ , F, Cl,  $\text{CH}_3$ ,  $\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}(\text{CH}_3)_2$ , -CN,  
 $\text{NO}_2$ ,  $\text{NR}^3\text{R}^{3a}$ ,  $\text{CH}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{C(O)R}^3$ ,  $\text{CH}_2\text{-C(O)R}^3$ ,  $\text{C(O)OR}^{3c}$ ,  
 $\text{CH}_2\text{-C(O)OR}^{3c}$ ,  $\text{NR}^3\text{C(O)R}^{3a}$ ,  $\text{CH}_2\text{NR}^3\text{C(O)R}^{3a}$ ,  $\text{C(O)NR}^3\text{R}^{3a}$ ,  $\text{CH}_2\text{-}$   
 $\text{C(O)NR}^3\text{R}^{3a}$ ,  $\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{CH}_2\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{SO}_2\text{-C}_{1-4}$  alkyl,  
 $\text{CH}_2\text{NR}^3\text{SO}_2\text{-C}_{1-4}$  alkyl,  $\text{NR}^3\text{SO}_2\text{-phenyl}$ ,  $\text{CH}_2\text{NR}^3\text{SO}_2\text{-phenyl}$ ,  
 10  $\text{S(O)}_p\text{CF}_3$ ,  $\text{CH}_2\text{S(O)}_p\text{CF}_3$ ,  $\text{S(O)}_p\text{-C}_{1-4}$  alkyl,  $\text{CH}_2\text{S(O)}_p\text{-C}_{1-4}$   
 alkyl,  $\text{S(O)}_p\text{-phenyl}$ ,  $\text{CH}_2\text{S(O)}_p\text{-phenyl}$ , and  $\text{CF}_3$ ;

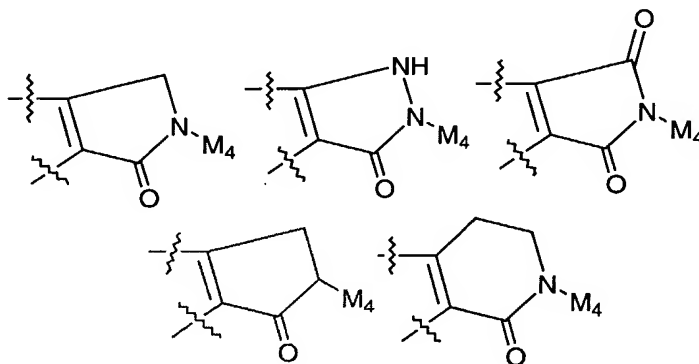
$\text{R}^{4c}$ , at each occurrence, is selected from =O,  $\text{OR}^2$ ,  
 $(\text{CR}^3\text{R}^{3a})\text{OR}^2$ , F,  $(\text{CR}^3\text{R}^{3a})\text{F}$ , Br,  $(\text{CR}^3\text{R}^{3a})\text{Br}$ , Cl,  
 15  $(\text{CR}^3\text{R}^{3a})\text{Cl}$ ,  $\text{CF}_3$ ,  $(\text{CR}^3\text{R}^{3a})\text{CF}_3$ ,  $\text{C}_{1-4}$  alkyl,  $\text{C}_{2-3}$  alkenyl,  
 $\text{C}_{2-3}$  alkynyl, -CN,  $(\text{CR}^3\text{R}^{3a})\text{CN}$ ,  $\text{NO}_2$ ,  $(\text{CR}^3\text{R}^{3a})\text{NO}_2$ ,  $\text{NR}^{2a}\text{R}^{2a}$ ,  
 $(\text{CR}^3\text{R}^{3a})\text{NR}^{2a}\text{R}^{2a}$ ,  $\text{N}(\rightarrow\text{O})\text{R}^{2a}\text{R}^{2a}$ ,  $(\text{CR}^3\text{R}^{3a})\text{N}(\rightarrow\text{O})\text{R}^{2a}\text{R}^{2a}$ ,  $\text{C(O)R}^{2c}$ ,  
 $(\text{CR}^3\text{R}^{3a})\text{C(O)R}^{2c}$ ,  $\text{NR}^{2b}\text{C(O)R}^{2b}$ ,  $(\text{CR}^3\text{R}^{3a})\text{NR}^{2b}\text{C(O)R}^{2b}$ ,  
 $\text{C(O)NR}^{2a}\text{R}^{2a}$ ,  $(\text{CR}^3\text{R}^{3a})\text{C(O)NR}^{2a}\text{R}^{2a}$ ,  $\text{NR}^{2b}\text{C(O)NR}^{2a}\text{R}^{2a}$ ,  
 20  $(\text{CR}^3\text{R}^{3a})\text{NR}^{2b}\text{C(O)NR}^{2a}\text{R}^{2a}$ ,  $\text{SO}_2\text{NR}^{2a}\text{R}^{2a}$ ,  $(\text{CR}^3\text{R}^{3a})\text{SO}_2\text{NR}^{2a}\text{R}^{2a}$ ,  
 $\text{NR}^{2a}\text{SO}_2\text{NR}^{2a}\text{R}^{2a}$ ,  $(\text{CR}^3\text{R}^{3a})\text{NR}^{2a}\text{SO}_2\text{NR}^{2a}\text{R}^{2a}$ ,  $\text{NR}^{2a}\text{SO}_2\text{R}^{5a}$ ,  
 $(\text{CR}^3\text{R}^{3a})\text{NR}^{2a}\text{SO}_2\text{R}^{5a}$ ,  $\text{S(O)}_p\text{R}^{5a}$ ,  $(\text{CR}^3\text{R}^{3a})\text{S(O)}_p\text{R}^{5a}$ ,  $\text{CF}_3$ ,  
 $\text{CF}_2\text{CF}_3$ ,  $\text{C}_{3-10}$  carbocycle substituted with 0-2  $\text{R}^{4b}$ ,  
 $(\text{CR}^3\text{R}^{3a})\text{-C}_{3-10}$  carbocycle substituted with 0-2  $\text{R}^{4b}$ , 5-10  
 25 membered heterocycle substituted with 0-2  $\text{R}^{4b}$  and  
 consisting of carbon atoms and from 1-4 heteroatoms  
 selected from the group consisting of N, O, and  $\text{S(O)}_p$ ,  
 and  $(\text{CR}^3\text{R}^{3a})\text{-5-10}$  membered heterocycle substituted with  
 0-2  $\text{R}^{4b}$  and consisting of carbon atoms and from 1-4  
 30 heteroatoms selected from the group consisting of N,  
 O, and  $\text{S(O)}_p$ ;

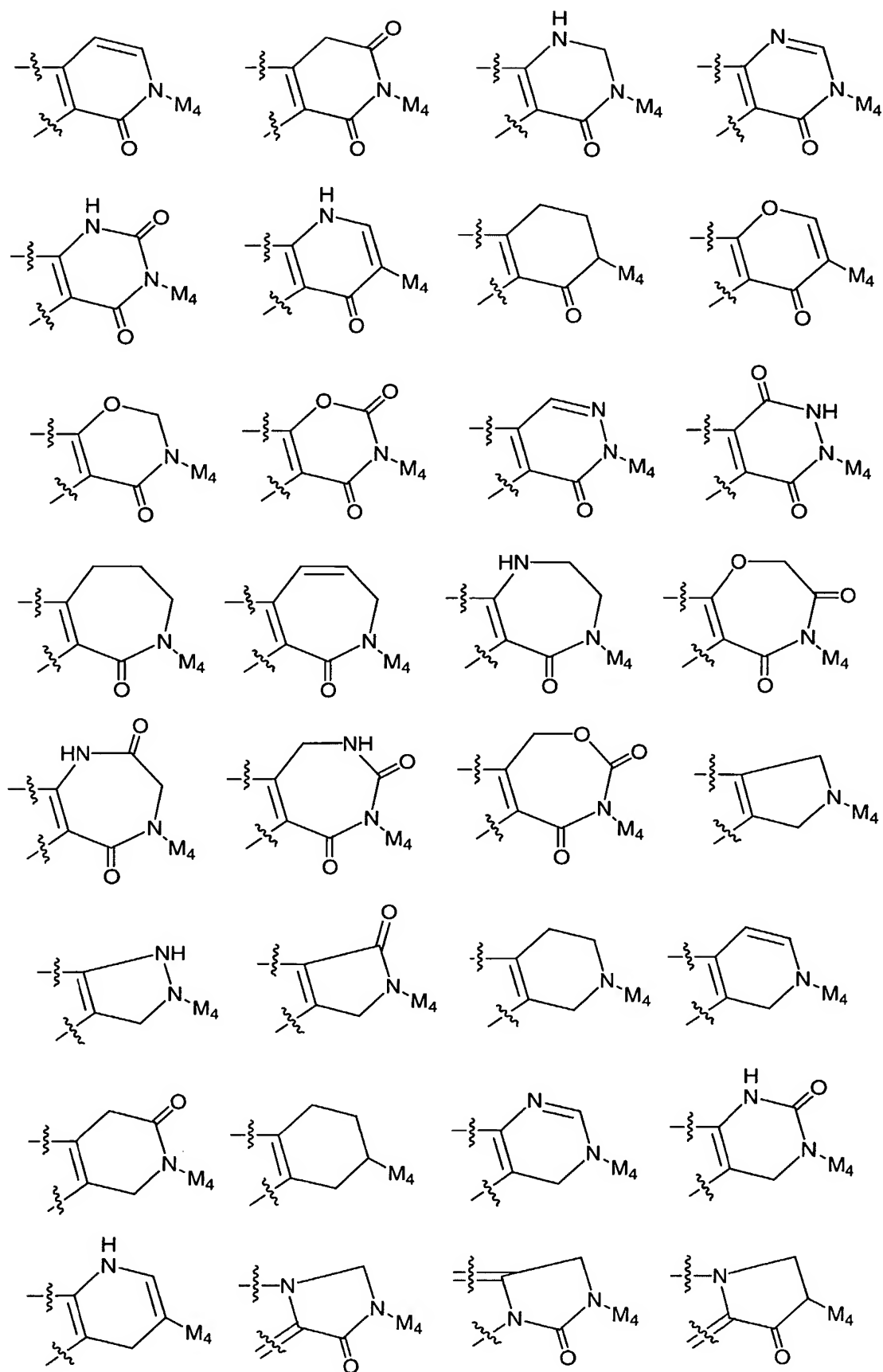
- $R^5$ , at each occurrence, is selected from H, =O,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $OR^3$ ,  $CH_2OR^3$ , F, Cl, -CN,  $NO_2$ ,  $NR^3R^{3a}$ ,  $CH_2NR^3R^{3a}$ ,  $C(O)R^3$ ,  $CH_2C(O)R^3$ ,  $C(O)OR^{3c}$ ,  $CH_2C(O)OR^{3c}$ ,  $NR^3C(O)R^{3a}$ ,  $C(O)NR^3R^{3a}$ ,  $SO_2NR^3R^{3a}$ ,  
 5  $NR^3SO_2-C_{1-4}$  alkyl,  $NR^3SO_2CF_3$ ,  $NR^3SO_2$ -phenyl,  $S(O)_pCF_3$ ,  $S(O)_p-C_{1-4}$  alkyl,  $S(O)_p$ -phenyl,  $CF_3$ , phenyl substituted with 0-2  $R^6$ , naphthyl substituted with 0-2  $R^6$ , and benzyl substituted with 0-2  $R^6$ ; and,
- 10  $R^6$ , at each occurrence, is selected from H, OH,  $OR^2$ , F, Cl,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , -CN,  $NO_2$ ,  $NR^2R^{2a}$ ,  $CH_2NR^2R^{2a}$ ,  $C(O)R^{2b}$ ,  $CH_2C(O)R^{2b}$ ,  $NR^2C(O)R^{2b}$ ,  $SO_2NR^2R^{2a}$ , and  $NR^2SO_2C_{1-4}$  alkyl.

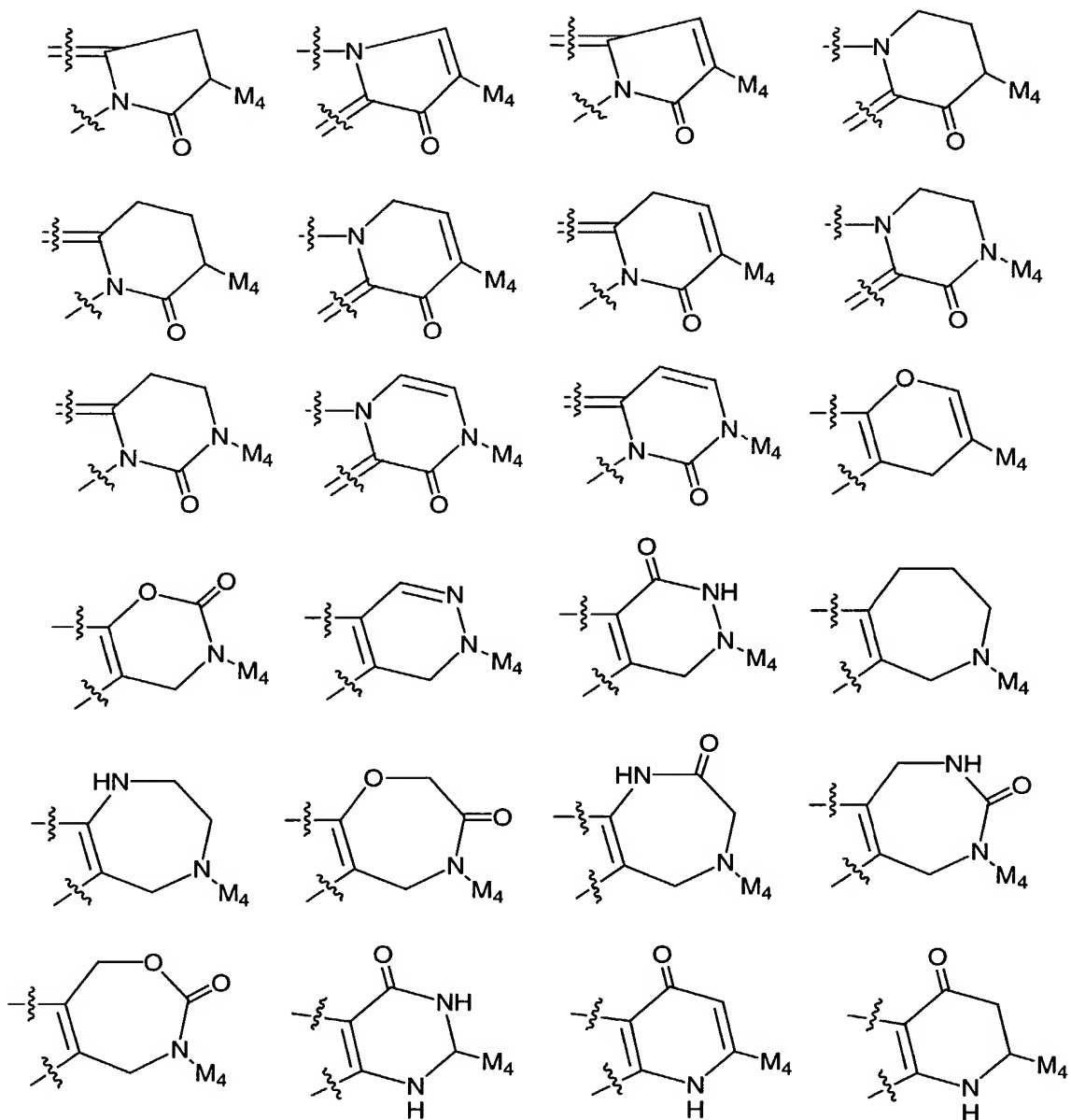
15

[4] In another preferred embodiment, the present invention provides a novel compound, wherein:

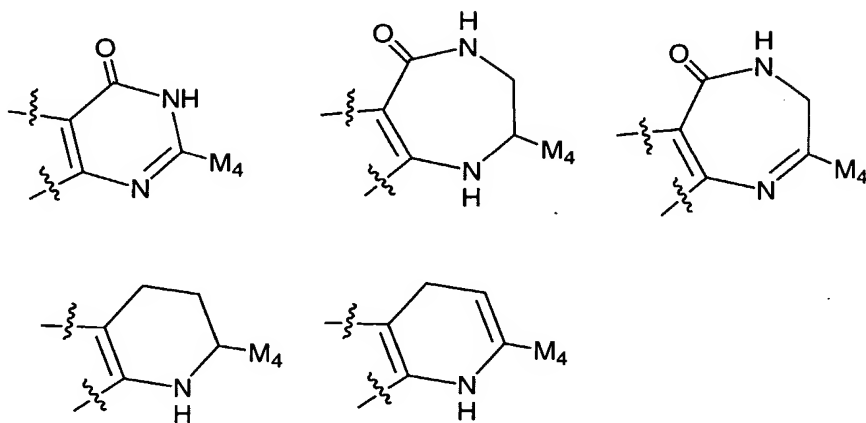
ring M is substituted with 0-2  $R^{1a}$  and is selected from the  
 20 group:







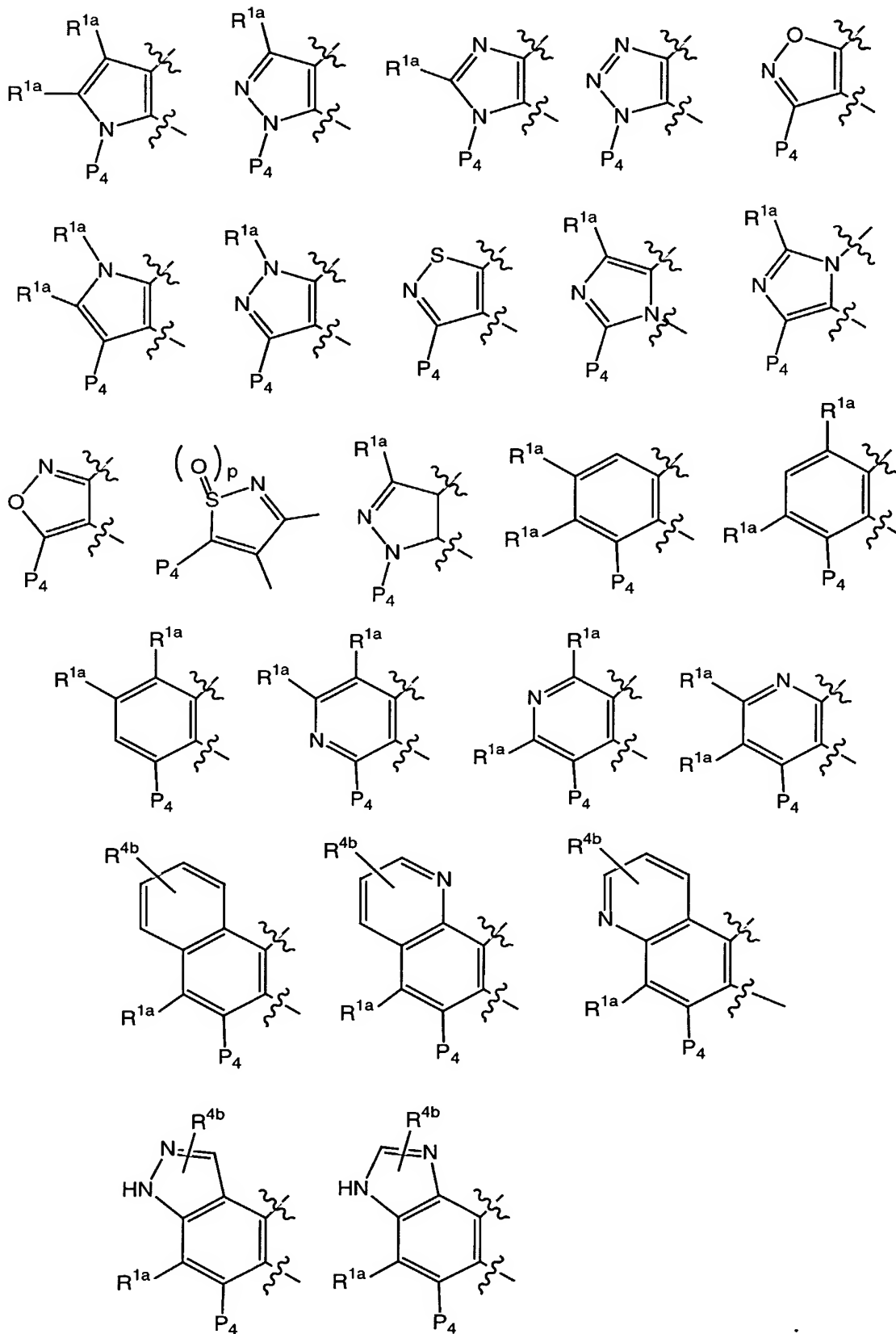
5



;

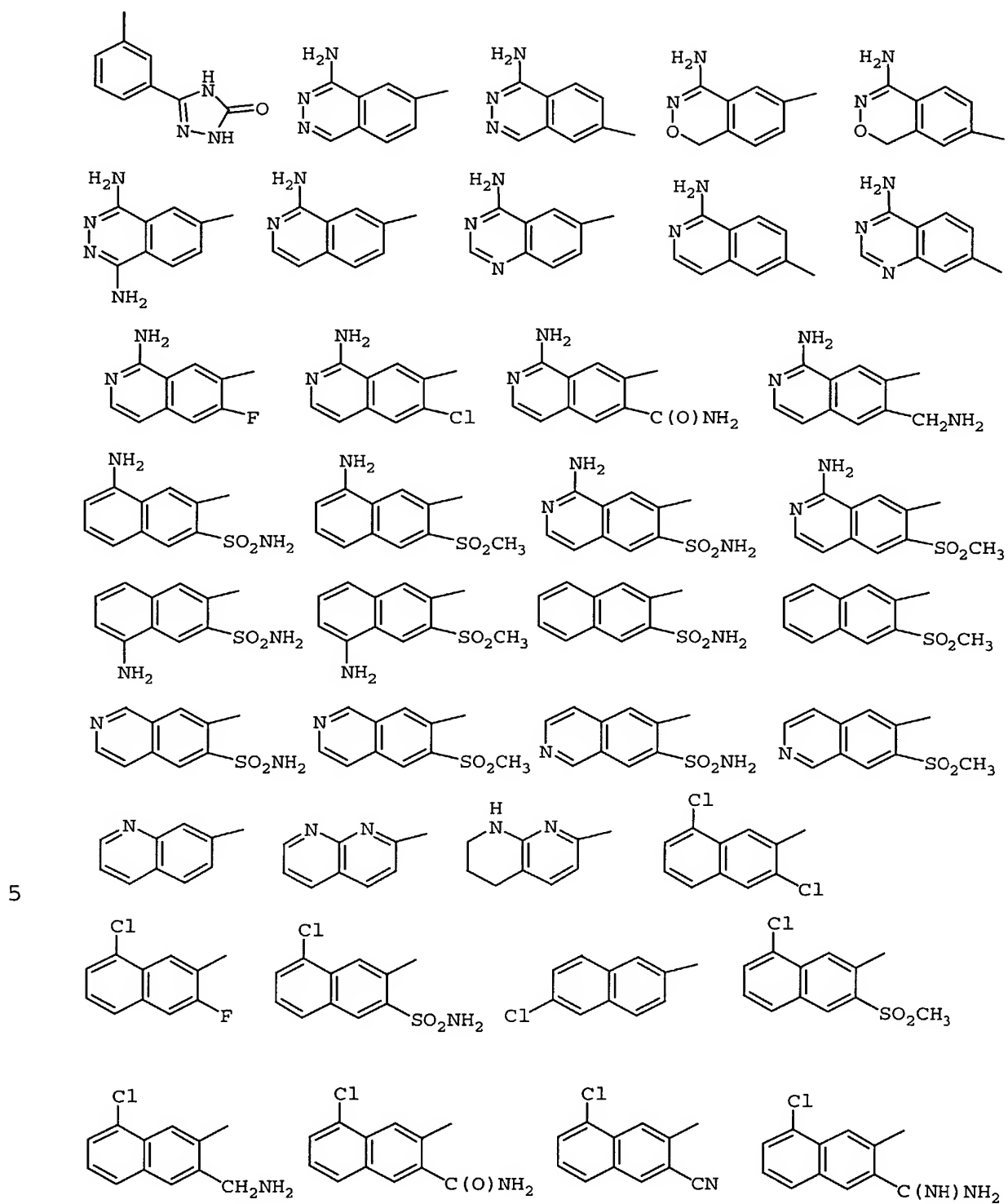


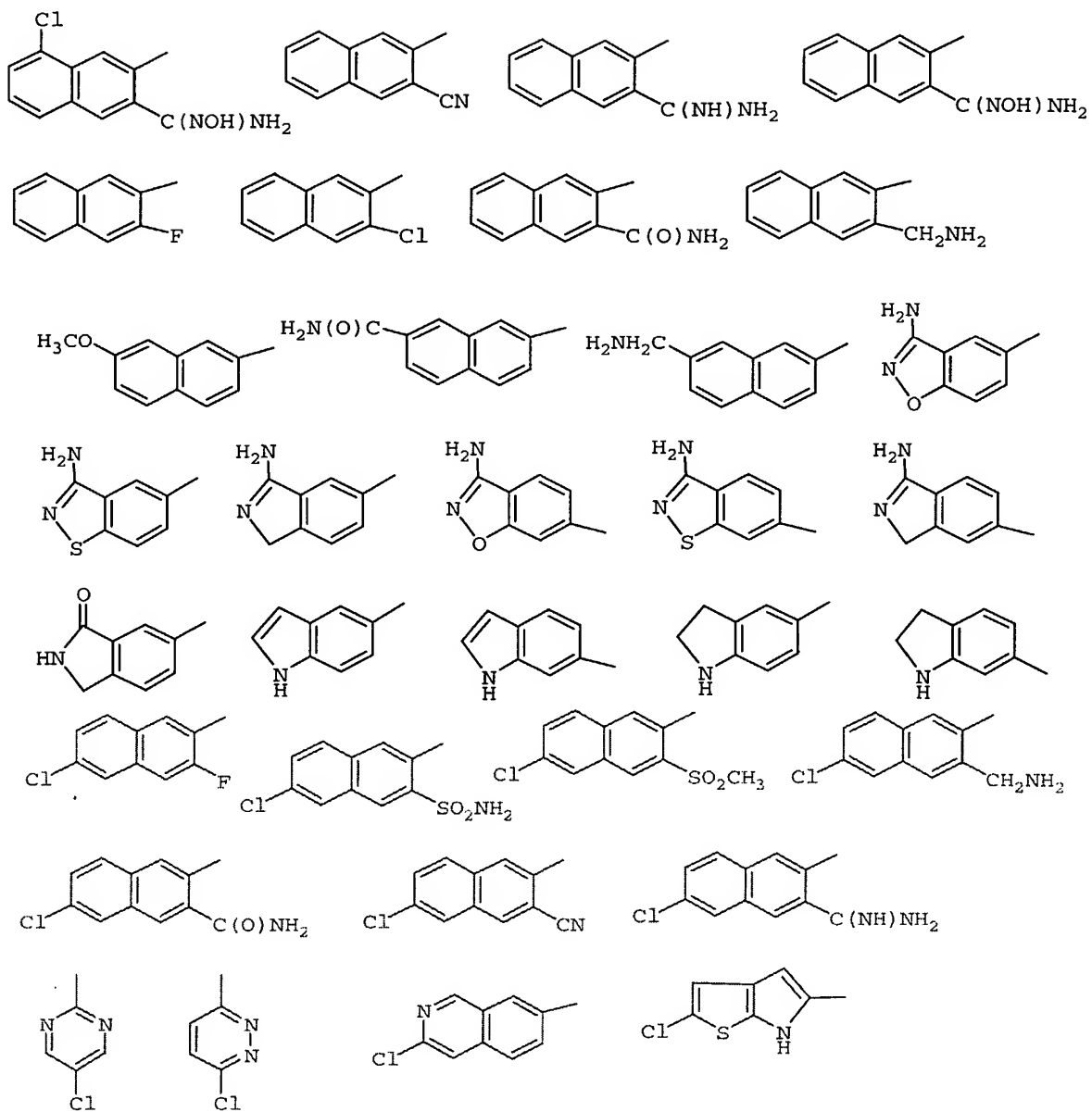
ring P, including P<sub>1</sub>, P<sub>2</sub>, P<sub>3</sub>, and P<sub>4</sub> is selected from group:

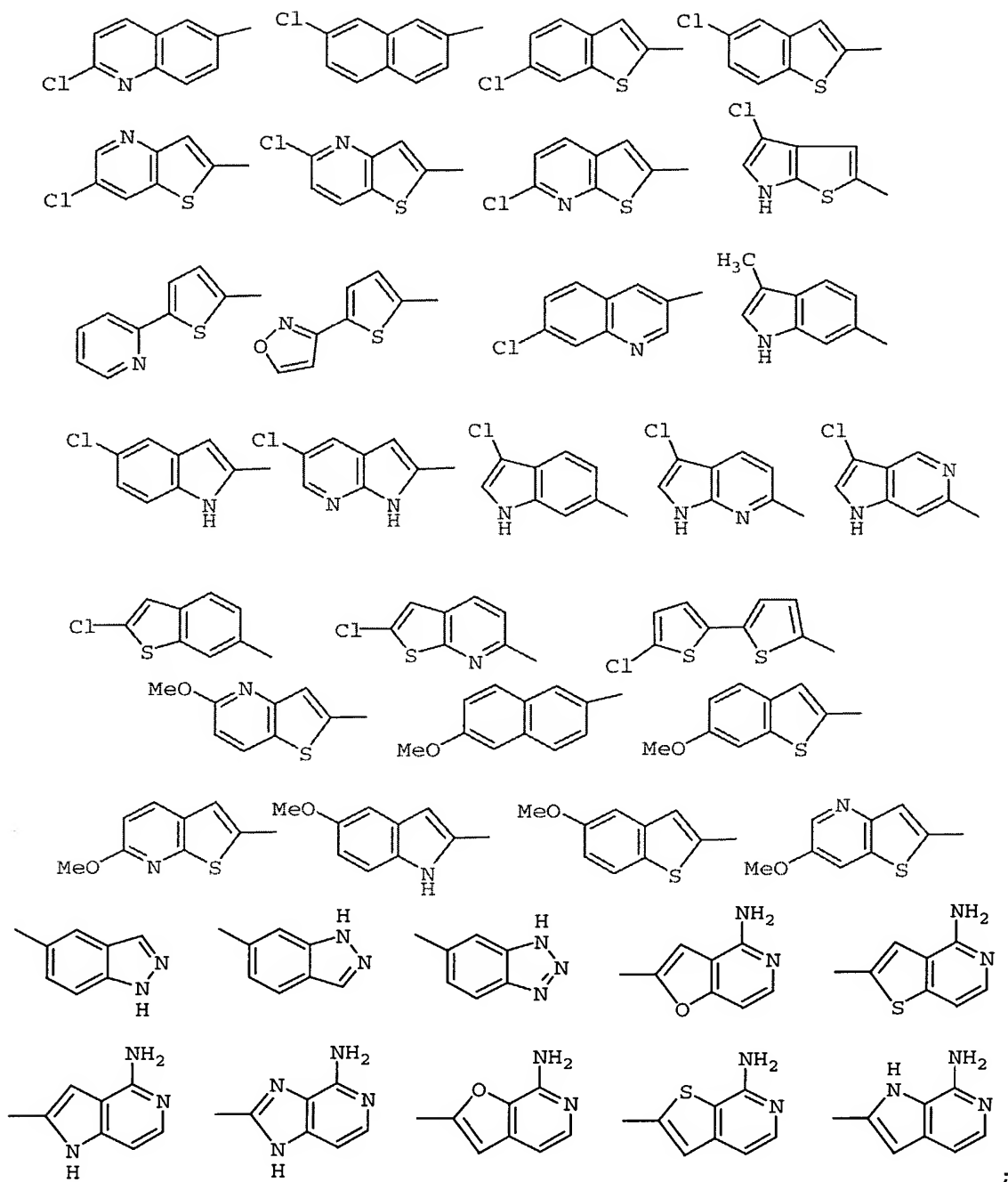


G is selected from the group:

- phenyl; 2-amido-4-methoxy-phenyl; 2-amido-phenyl;  
2-aminomethyl-3-fluoro-phenyl;  
5 2-aminomethyl-4-fluoro-phenyl;  
2-aminomethyl-4-methoxy-phenyl;  
2-aminomethyl-5-fluoro-phenyl;  
2-aminomethyl-5-methoxy-phenyl;  
2-aminomethyl-6-fluoro-phenyl; 2-aminomethyl-phenyl;  
10 2-amino-pyrid-4-yl; 2-aminosulfonyl-4-methoxy-phenyl;  
2-aminosulfonyl-phenyl; 2-methylsulfonyl-phenyl; 2-  
aminomethyl-4-ethyl-phenyl; 2-aminosulfonyl-4-ethyl-phenyl;  
2-amido-4-ethyl-phenyl;  
3-(N,N-dimethylamino)-4-chloro-phenyl;  
15 3-(N,N-dimethylamino)-phenyl;  
3-(N-methylamino)-4-chloro-phenyl;  
3-(N-methylamino)-phenyl; 3-amido-phenyl;  
3-amino-4-chloro-phenyl; 3-aminomethyl-phenyl;  
3-amino-phenyl; 3-chloro-phenyl;  
20 4-(N,N-dimethylamino)-5-chloro-thien-2-yl;  
4-(N-methylamino)-5-chloro-thien-2-yl;  
4-amino-5-chloro-thien-2-yl; 4-chloro-phenyl; 4-ethyl-  
phenyl; 4-ethyl-2-methylsulfonyl-phenyl; 4-ethyl-2-methoxy-  
phenyl; 4-methoxy-2-methylsulfonyl-phenyl;  
25 4-methoxy-phenyl;  
5-(N,N-dimethylamino)-4-chloro-thien-2-yl;  
5-(N-methylamino)-4-chloro-thien-2-yl;  
5-amino-4-chloro-thien-2-yl; 5-chloro-pyrid-2-yl;  
5-chloro-thien-2-yl; 5-methoxy-thien-2-yl;  
30 5-methyl-thien-2-yl; 5-fluoro-thien-2-yl;  
6-amino-5-chloro-pyrid-2-yl; 6-amino-pyrid-2-yl;







5  $G_1$  is absent or is selected from  $CH_2$ ,  $CH_2CH_2$ ,  $CH=CH$ ,  $CH_2O$ ,  
 $OCH_2$ ,  $NH$ ,  $CH_2NH$ ,  $NHCH_2$ ,  $CH_2C(O)$ ,  $C(O)CH_2$ ,  $C(O)NH$ ,  
 $NHC(O)$ ,  $CH_2S(O)_2$ ,  $S(O)_2(CH_2)$ ,  $SO_2NH$ , and  $NHSO_2$ ,  
provided that  $G_1$  does not form a N-S,  $NCH_2N$ ,  $NCH_2O$ , or  
 $NCH_2S$  bond with either group to which it is attached;

A is selected from cyclohexyl, piperidinyl, phenyl, pyridyl, and pyrimidyl, and is substituted with 0-2  $R^4$ ;

5 X is selected from  $CH_2$ ,  $C(O)$ ,  $-S(O)_2-$ ,  $-NHC(O)-$ ,  $-C(O)NH-$ ,  $-CH_2NH-$ , O, and  $-CH_2O-$ ;

Y is selected from  $C(CH_3)_2$ ,  $C(CH_2CH_3)_2$ , cyclopropyl, cyclobutyl, cyclopentyl, cyclopentanonyl, cyclohexyl, cyclohexanonyl, pyrrolidinyl, pyrrolidinonyl, 10 piperidinyl, piperidinonyl, tetrahydrofuranyl, and tetrahydropyranyl, and, when Y is a ring, Y is substituted with 0-1  $R^4$ ;

15  $R^{1a}$ , at each occurrence, is selected from H,  $R^{1b}$ ,  $CH(CH_3)R^{1b}$ ,  $C(CH_3)_2R^{1b}$ , and  $CH_2R^{1b}$ , provided that  $R^{1a}$  forms other than an N-halo, N-S, or N-CN bond;

$R^{1b}$  is selected from  $CH_3$ ,  $CH_2CH_3$ , F, Cl, Br,  $-CN$ ,  $CF_3$ ,  $OR^2$ , 20  $NR^2R^{2a}$ ,  $C(O)R^{2b}$ ,  $CO_2R^{2b}$ ,  $CO_2R^{2a}$ ,  $S(O)_pR^2$ ,  $C(O)NR^2R^{2a}$ ,  $SO_2NR^2R^{2a}$ ,  $NR^2SO_2R^2$ , and 5-6 membered aromatic heterocycle consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$  and substituted with 0-2  $R^{4b}$ , provided 25 that  $R^{1b}$  forms other than an O-O, N-halo, N-S, or N-CN bond;

$R^2$ , at each occurrence, is selected from H,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ , phenyl substituted with 0-1  $R^{4b}$ , 30 benzyl substituted with 0-1  $R^{4b}$ , and 5-6 membered aromatic heterocycle substituted with 0-1  $R^{4b}$  and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and  $S(O)_p$ ;

R<sup>2a</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, benzyl, phenyl substituted with 0-1 R<sup>4b</sup>, and 5-6 membered aromatic heterocycle substituted with 0-1 R<sup>4b</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the nitrogen atom to which they are attached, combine to form a 5 or 6 membered saturated, partially saturated or unsaturated ring substituted with 0-1 R<sup>4b</sup> and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2b</sup>, at each occurrence, is selected from OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, benzyl, phenyl substituted with 0-1 R<sup>4b</sup>, and 5-6 membered aromatic heterocycle substituted with 0-1 R<sup>4b</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2c</sup>, at each occurrence, is selected from OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, benzyl, phenyl substituted with 0-1 R<sup>4b</sup>, and 5-6 membered aromatic heterocycle substituted with 0-1 R<sup>4b</sup> and consisting of carbon atoms and from 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

R<sup>2d</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl substituted with 0-2 R<sup>4c</sup>, C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, -(CH<sub>2</sub>)-C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, 5-6 membered heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of: carbon atoms and 1-4

heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and -(CH<sub>2</sub>)-5-6 membered heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2d</sup> forms other than a N-halo, N-C-halo, S(O)<sub>p</sub>-halo, O-halo, N-S, S-N, S(O)<sub>p</sub>-S(O)<sub>p</sub>, S-O, O-N, O-S, or O-O moiety;

R<sup>2e</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl substituted with 0-2 R<sup>4c</sup>, C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, -(CH<sub>2</sub>)-C<sub>3-6</sub> carbocycle substituted with 0-2 R<sup>4c</sup>, 5-6 membered heterocycle substituted with 0-2 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, and -(CH<sub>2</sub>)-5-6 membered heterocycle and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2e</sup> forms other than a C(O)-halo or C(O)-S(O)<sub>p</sub> moiety;

R<sup>4</sup>, at each occurrence, is selected from OH, OR<sup>2</sup>, CH<sub>2</sub>OR<sup>2</sup>, (CH<sub>2</sub>)<sub>2</sub>OR<sup>2</sup>, F, Br, Cl, I, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH(CH<sub>3</sub>)<sub>2</sub>, CH(CH<sub>3</sub>)CH<sub>2</sub>CH<sub>3</sub>, C(CH<sub>3</sub>)<sub>3</sub>, NR<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, (CH<sub>2</sub>)<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, CF<sub>3</sub>, and CF<sub>2</sub>CF<sub>3</sub>;

R<sup>4a</sup> is selected from -(CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-5-6 membered carbocycle substituted with 0-3 R<sup>4c</sup>, -(CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-5-6 membered heterocycle substituted with 0-3 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>NR<sup>2d</sup>R<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>N(→O)R<sup>2d</sup>R<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>OR<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-C(O)NR<sup>2d</sup>R<sup>2d</sup>, (CR<sup>3</sup>R<sup>3g</sup>)<sub>r</sub>-NR<sup>2d</sup>C(O)R<sup>2e</sup>,



$(\text{CR}^3\text{R}^3\text{g})_r\text{-C(O)R}^{2e}$ ,  $(\text{CR}^3\text{R}^3\text{g})_r\text{-NR}^{2d}\text{C(O)NR}^{2d}\text{R}^{2d}$ ,  
 $(\text{CR}^3\text{R}^3\text{g})_r\text{-NR}^{2d}\text{C(O)OR}^{2d}$ ,  $(\text{CR}^3\text{R}^3\text{g})_r\text{-NR}^{2d}\text{SO}_2\text{R}^{2d}$ , and  
 $(\text{CR}^3\text{R}^3\text{g})_r\text{-S(O)}_p\text{R}^{2d}$ , provided that  $\text{S(O)}_p\text{R}^{2d}$  forms other  
 than  $\text{S(O)}_2\text{H}$  or  $\text{S(O)H}$ ;

5

$\text{R}^{4b}$ , at each occurrence, is selected from H, =O,  $\text{OR}^3$ ,  
 $\text{CH}_2\text{OR}^3$ , F, Cl,  $\text{CH}_3$ ,  $\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}(\text{CH}_3)_2$ , -CN,  
 $\text{NO}_2$ ,  $\text{NR}^3\text{R}^{3a}$ ,  $\text{CH}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{C(O)R}^3$ ,  $\text{C(O)OR}^{3c}$ ,  $\text{NR}^3\text{C(O)R}^{3a}$ ,  
 $\text{C(O)NR}^3\text{R}^{3a}$ ,  $\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{SO}_2\text{-C}_{1-4}$  alkyl,  $\text{NR}^3\text{SO}_2\text{-phenyl}$ ,  
 $\text{S(O)}_p\text{-C}_{1-4}$  alkyl,  $\text{S(O)}_p\text{-phenyl}$ , and  $\text{CF}_3$ ;

10

$\text{R}^{4c}$ , at each occurrence, is selected from =O,  $\text{OR}^2$ ,  $\text{CH}_2\text{OR}^2$ ,  
 F, Br, Cl,  $\text{CF}_3$ ,  $\text{CH}_3$ ,  $\text{CH}_2\text{CH}_3$ ,  $\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}(\text{CH}_3)_2$ ,  $\text{C}_{2-3}$   
 alkenyl,  $\text{C}_{2-3}$  alkynyl, -CN,  $\text{NO}_2$ ,  $\text{NR}^{2d}\text{R}^{2a}$ ,  $\text{CH}_2\text{NR}^{2d}\text{R}^{2a}$ ,  
 $\text{N}(\rightarrow\text{O})\text{R}^{2d}\text{R}^{2a}$ ,  $\text{CH}_2\text{N}(\rightarrow\text{O})\text{R}^{2d}\text{R}^{2a}$ ,  $\text{C(O)R}^{2c}$ ,  $\text{CH}_2\text{C(O)R}^{2c}$ ,  
 $\text{NR}^{2d}\text{C(O)R}^{2b}$ ,  $\text{CH}_2\text{NR}^{2d}\text{C(O)R}^{2b}$ ,  $\text{C(O)NR}^{2d}\text{R}^{2a}$ ,  $\text{CH}_2\text{C(O)NR}^{2d}\text{R}^{2a}$ ,  
 $\text{SO}_2\text{NR}^{2d}\text{R}^{2a}$ ,  $\text{CH}_2\text{SO}_2\text{NR}^{2d}\text{R}^{2a}$ ,  $\text{NR}^{2d}\text{SO}_2\text{R}^{5a}$ ,  $\text{CH}_2\text{NR}^{2d}\text{SO}_2\text{R}^{5a}$ ,  
 $\text{S(O)}_p\text{R}^{5a}$ ,  $\text{CH}_2\text{S(O)}_p\text{R}^{5a}$ ,  $\text{CF}_3$ ,  $\text{CF}_2\text{CF}_3$ ,  $\text{C}_{3-6}$  carbocycle  
 substituted with 0-2  $\text{R}^{4b}$ ,  $(\text{CH}_2)\text{-C}_{3-6}$  carbocycle  
 substituted with 0-2  $\text{R}^{4b}$ , 5-6 membered heterocycle  
 substituted with 0-2  $\text{R}^{4b}$  and consisting of carbon atoms  
 and from 1-4 heteroatoms selected from the group  
 consisting of N, O, and  $\text{S(O)}_p$ , and  $(\text{CH}_2)\text{-5-6}$  membered  
 heterocycle substituted with 0-2  $\text{R}^{4b}$  and consisting of  
 carbon atoms and from 1-4 heteroatoms selected from  
 the group consisting of N, O, and  $\text{S(O)}_p$ ;

20

25

$\text{R}^5$ , at each occurrence, is selected from H, =O,  $\text{CH}_3$ ,  $\text{CH}_2\text{CH}_3$ ,  
 $\text{CH}_2\text{CH}_2\text{CH}_3$ ,  $\text{CH}(\text{CH}_3)_2$ ,  $\text{OR}^3$ ,  $\text{CH}_2\text{OR}^3$ , F, Cl, -CN,  $\text{NO}_2$ ,  
 $\text{NR}^3\text{R}^{3a}$ ,  $\text{CH}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{C(O)R}^3$ ,  $\text{C(O)OR}^{3c}$ ,  $\text{NR}^3\text{C(O)R}^{3a}$ ,  
 $\text{C(O)NR}^3\text{R}^{3a}$ ,  $\text{SO}_2\text{NR}^3\text{R}^{3a}$ ,  $\text{NR}^3\text{SO}_2\text{-C}_{1-4}$  alkyl,  $\text{NR}^3\text{SO}_2\text{-phenyl}$ ,  
 $\text{S(O)}_p\text{-C}_{1-4}$  alkyl,  $\text{S(O)}_p\text{-phenyl}$ ,  $\text{CF}_3$ , phenyl substituted

30

with 0-2  $R^6$ , naphthyl substituted with 0-2  $R^6$ , and  
benzyl substituted with 0-2  $R^6$ ;

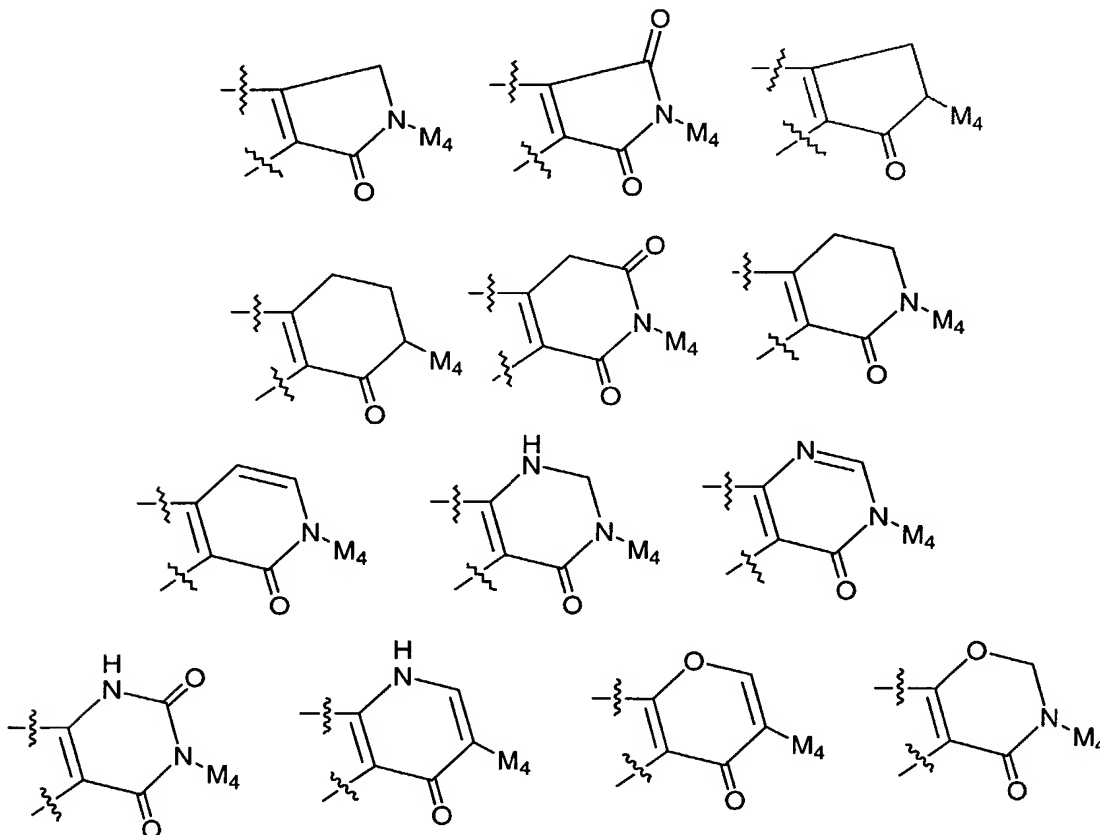
$R^6$ , at each occurrence, is selected from H, OH,  $OR^2$ , F, Cl,  
5  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $-CN$ ,  $NO_2$ ,  $NR^2R^{2a}$ ,  
 $CH_2NR^2R^{2a}$ ,  $C(O)R^{2b}$ ,  $CH_2C(O)R^{2b}$ ,  $NR^2C(O)R^{2b}$ , and  
 $SO_2NR^2R^{2a}$ ; and,

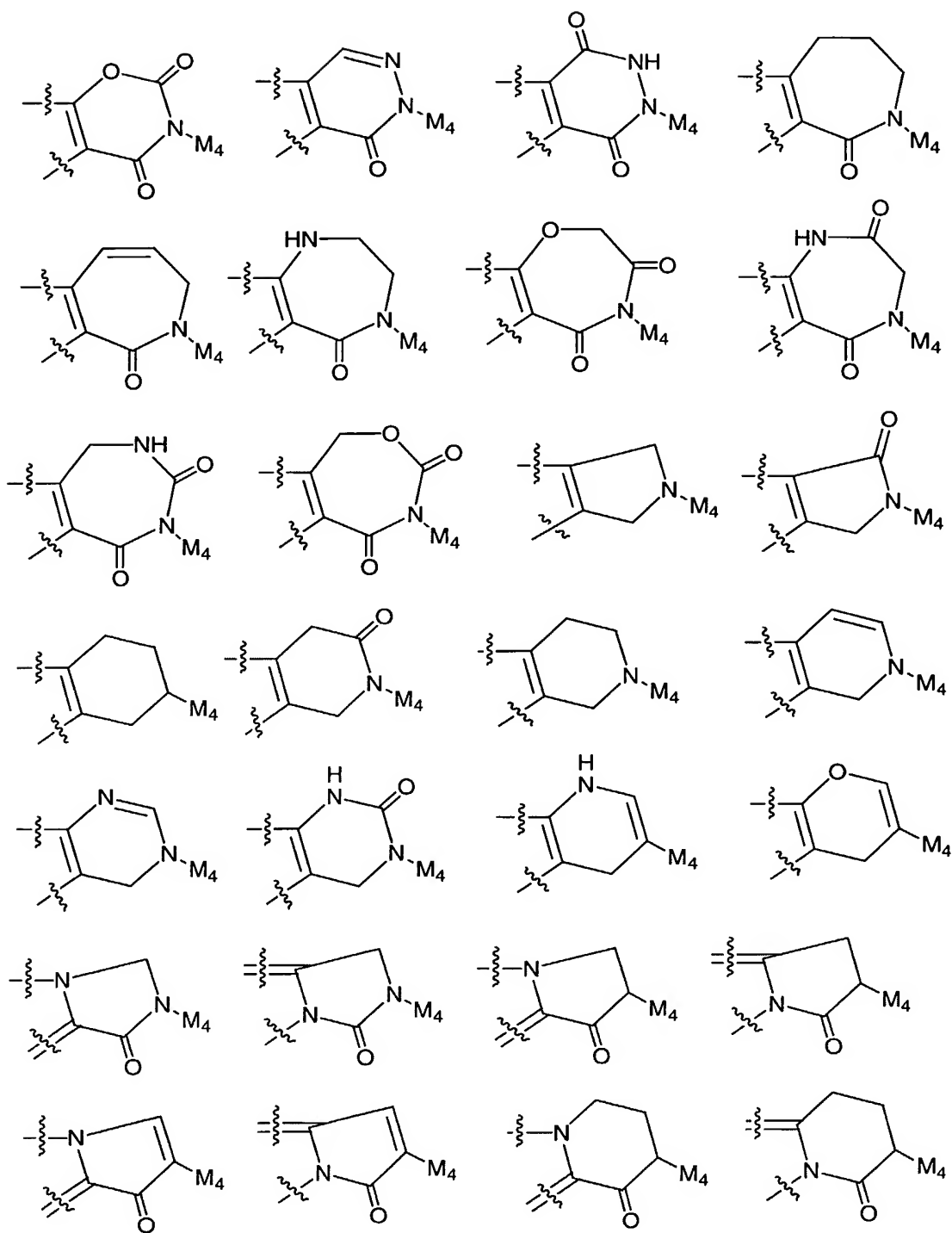
r, at each occurrence, is selected from 0, 1, and 2.

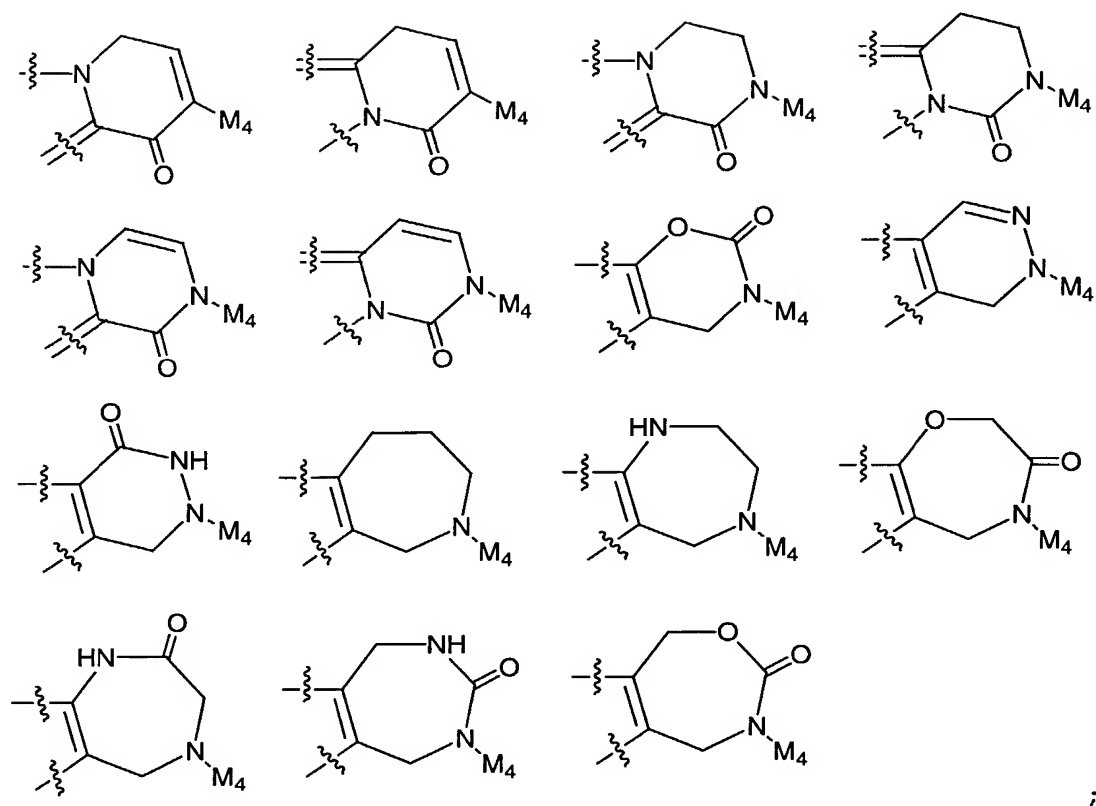
10

[5] In another preferred embodiment, the present invention  
provides a novel compound, wherein:

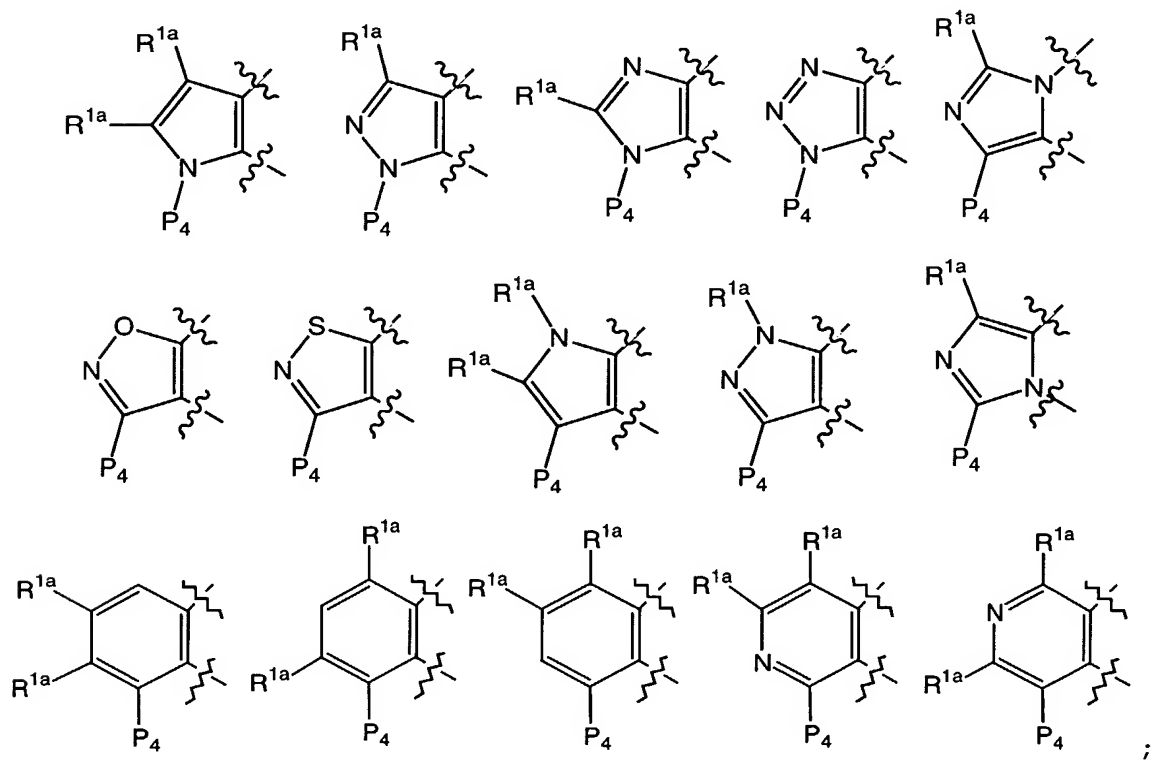
15 ring M is substituted with 0-1  $R^{1a}$  and is selected from the  
group:





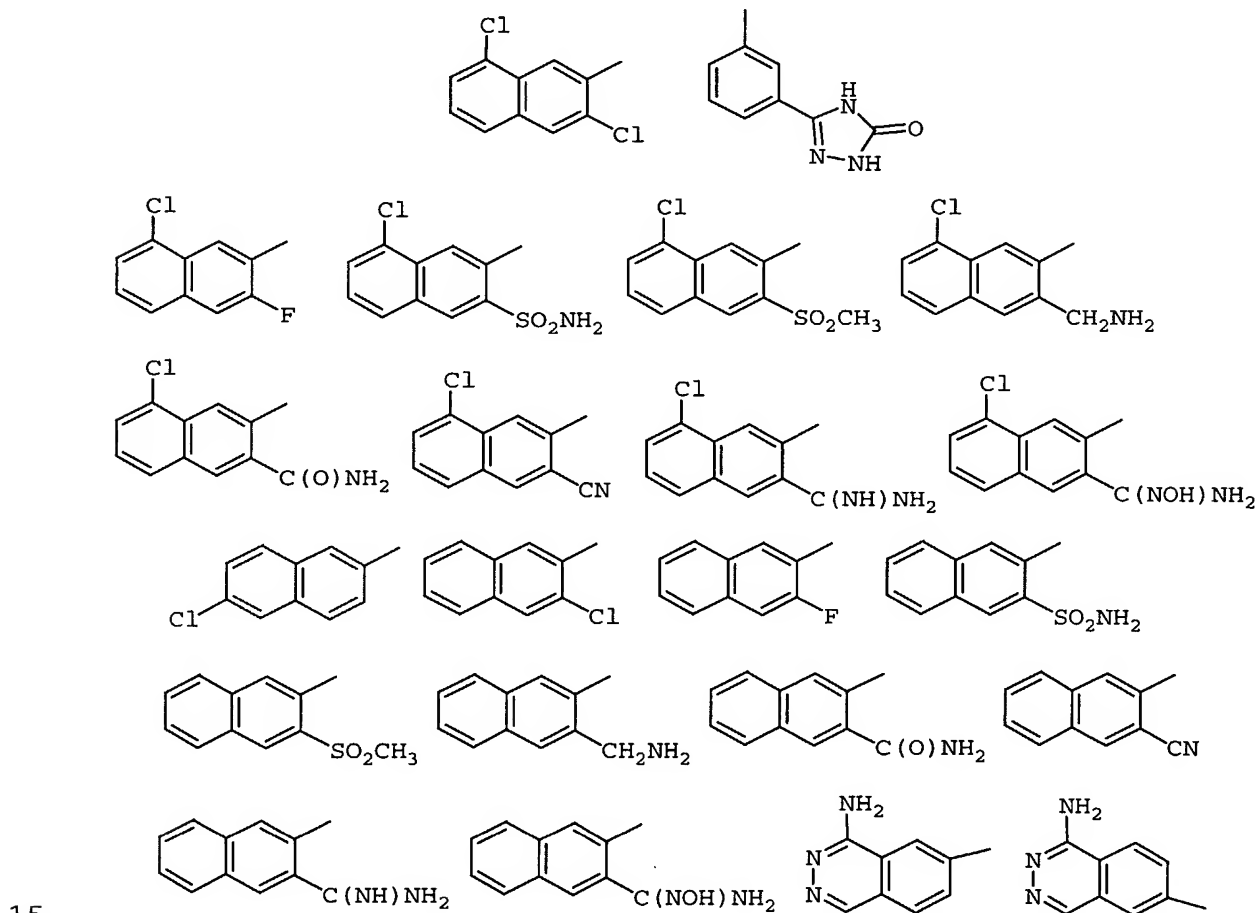


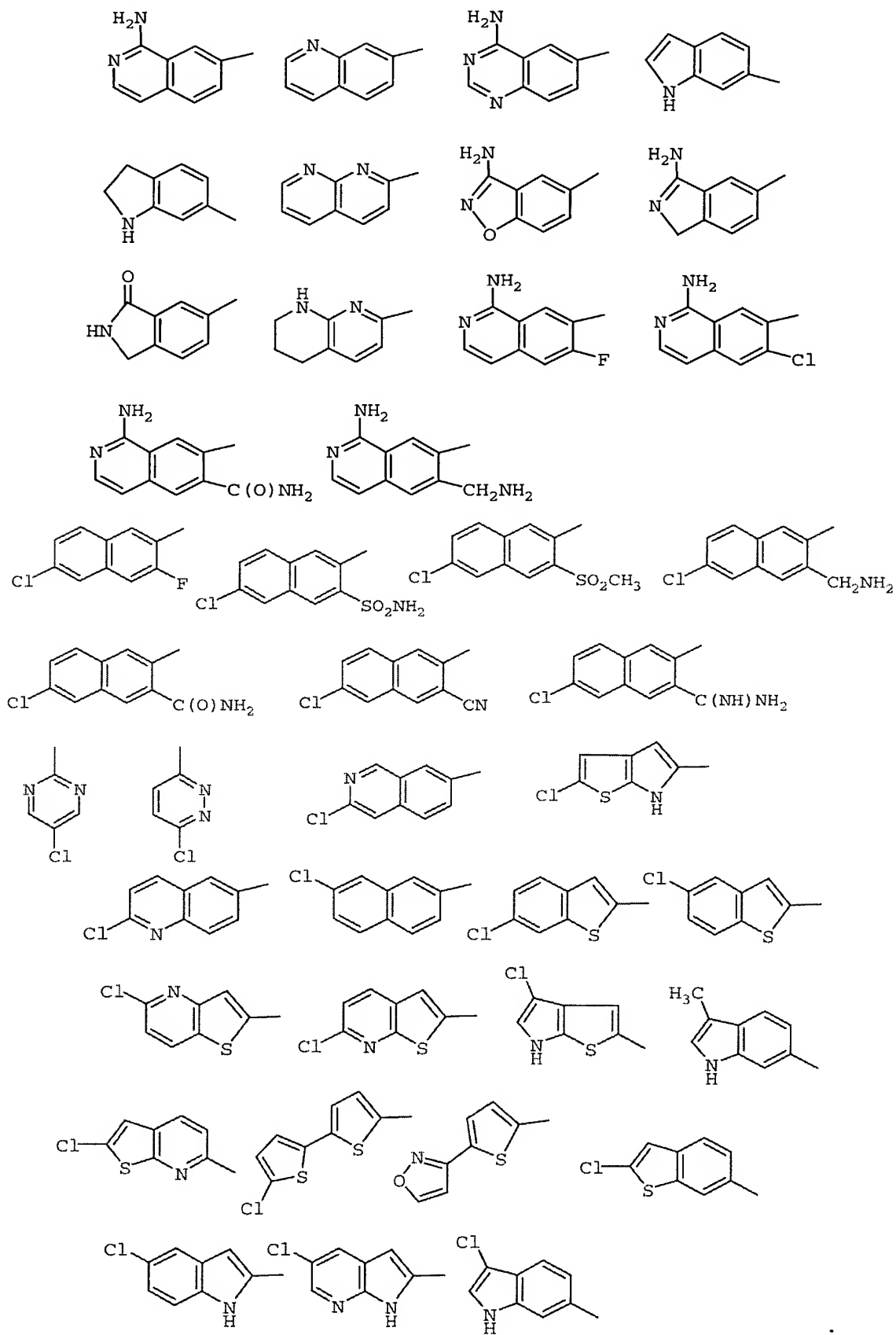
ring P, including P<sub>1</sub>, P<sub>2</sub>, P<sub>3</sub>, and P<sub>4</sub> is selected from group:



-G is selected from:

- 2-amido-4-methoxy-phenyl; 2-amido-phenyl;  
 2-aminomethyl-3-fluoro-phenyl;  
 2-aminomethyl-4-fluoro-phenyl;  
 5 2-aminomethyl-5-fluoro-phenyl;  
 2-aminomethyl-6-fluoro-phenyl; 2-aminomethyl-phenyl;  
 2-amino-pyrid-4-yl; 2-aminosulfonyl-4-methoxy-phenyl;  
 2-aminosulfonyl-phenyl; 3-amido-phenyl;  
 3-amino-4-chloro-phenyl; 3-aminomethyl-phenyl;  
 10 3-chloro-phenyl; 4-chloro-phenyl; 4-ethyl-phenyl;  
 4-methoxy-phenyl; 5-chloro-pyrid-2-yl; 5-chloro-thien-2-yl;  
 6-amino-5-chloro-pyrid-2-yl; 6-amino-pyrid-2-yl;





;

A is selected from the group: cyclohexyl, piperidiny1, phenyl, 2-pyridyl, 3-pyridyl, 2-pyrimidyl, 2-Cl-phenyl, 3-Cl-phenyl, 2-F-phenyl, 3-F-phenyl, 2-methylphenyl, 2-aminophenyl, and 2-methoxyphenyl;

5

Y is selected from C(CH<sub>3</sub>)<sub>2</sub>, C(CH<sub>2</sub>CH<sub>3</sub>)<sub>2</sub>, cyclopropyl, cyclobutyl, cyclopentyl, 2-cyclopentanonyl, cyclohexyl, 2-cyclohexanonyl, pyrrolidinyl (attached to A and R<sup>4a</sup> at the 2-position), pyrrolidinyl (attached to A and R<sup>4a</sup> at the 3-position), 2-pyrrolidinonyl (attached to A and R<sup>4a</sup> at the 3-position), piperidiny1 (attached to A and R<sup>4a</sup> at the 4-position), 4-piperidinonyl (attached to A and R<sup>4a</sup> at the 3-position), tetrahydrofuranyl, and tetrahydropyranyl (attached to A and R<sup>4a</sup> at the 4-position);

10

15

R<sup>1a</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>F, CH<sub>2</sub>Cl, Br, CH<sub>2</sub>Br, -CN, CH<sub>2</sub>CN, CF<sub>3</sub>, CH<sub>2</sub>CF<sub>3</sub>, OCH<sub>3</sub>, CH<sub>2</sub>OH, C(CH<sub>3</sub>)<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, NH<sub>2</sub>, CH<sub>2</sub>NH<sub>2</sub>, NHCH<sub>3</sub>, CH<sub>2</sub>NHCH<sub>3</sub>, N(CH<sub>3</sub>)<sub>2</sub>, CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, CO<sub>2</sub>H, COCH<sub>3</sub>, CO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CO<sub>2</sub>CH<sub>3</sub>, SCH<sub>3</sub>, CH<sub>2</sub>SCH<sub>3</sub>, S(O)CH<sub>3</sub>, CH<sub>2</sub>S(O)CH<sub>3</sub>, S(O)<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>S(O)<sub>2</sub>CH<sub>3</sub>, C(O)NH<sub>2</sub>, CH<sub>2</sub>C(O)NH<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, CH<sub>2</sub>SO<sub>2</sub>NH<sub>2</sub>, NHSO<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>NHSO<sub>2</sub>CH<sub>3</sub>, pyridin-2-yl, pyridin-3-yl, pyridin-4-yl, pyridin-2-yl-N-oxide, pyridin-3-yl-N-oxide, pyridin-4-yl-N-oxide, imidazol-1-yl, CH<sub>2</sub>-imidazol-1-yl, 4-methyl-oxazol-2-yl, 4-N,N-dimethylaminomethyl-oxazol-2-yl, 1,2,3,4-tetrazol-1-yl, 1,2,3,4-tetrazol-5-yl, CH<sub>2</sub>-1,2,3,4-tetrazol-1-yl, and CH<sub>2</sub>-1,2,3,4-tetrazol-5-yl, provided that R<sup>1a</sup> forms other than an N-halo, N-S, or N-CN bond;

20

25

R<sup>2</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, phenyl substituted with 0-1 R<sup>4b</sup>, benzyl substituted with 0-1 R<sup>4b</sup>, and 5 membered

aromatic heterocycle substituted with 0-1 R<sup>4b</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

- 5 R<sup>2a</sup>, at each occurrence, is selected from H, CH<sub>3</sub>, and CH<sub>2</sub>CH<sub>3</sub>;

alternatively, R<sup>2</sup> and R<sup>2a</sup>, together with the nitrogen atom to which they are attached, combine to form a 5 or 6  
10 membered saturated, partially saturated or unsaturated ring substituted with 0-1 R<sup>4b</sup> and consisting of: 0-1 additional heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>;

- 15 R<sup>2b</sup>, at each occurrence, is selected from OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, CH<sub>3</sub>, and CH<sub>2</sub>CH<sub>3</sub>;

R<sup>2c</sup>, at each occurrence, is selected from OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, CH<sub>3</sub>, and CH<sub>2</sub>CH<sub>3</sub>;

20

- R<sup>2d</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl substituted with 0-2 R<sup>4c</sup>, C<sub>3-6</sub> cycloalkyl substituted with 0-2 R<sup>4c</sup>, phenyl substituted with 0-2 R<sup>4c</sup>, and 5-6 membered aromatic heterocycle substituted with 0-2 R<sup>4c</sup>  
25 and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2d</sup> forms other than a N-halo, N-C-halo, S(O)<sub>p</sub>-halo, O-halo, N-S, S-N, S(O)<sub>p</sub>-S(O)<sub>p</sub>, S-O, O-N, O-S, or O-O moiety;

30

- R<sup>2e</sup>, at each occurrence, is selected from H, R<sup>4c</sup>, C<sub>1-4</sub> alkyl substituted with 0-2 R<sup>4c</sup>, C<sub>3-6</sub> cycloalkyl substituted with 0-2 R<sup>4c</sup>, phenyl substituted with 0-2 R<sup>4c</sup>, and 5-6 membered aromatic heterocycle substituted with 0-2 R<sup>4c</sup>



and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2e</sup> forms other than a C(O)-halo or C(O)-S(O)<sub>p</sub> moiety;

5

R<sup>4a</sup> is selected from -(CH<sub>2</sub>)<sub>r</sub>-5-6 membered carbocycle substituted with 0-3 R<sup>4c</sup>, -(CH<sub>2</sub>)<sub>r</sub>-5-6 membered heterocycle substituted with 0-3 R<sup>4c</sup> and consisting of: carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, (CH<sub>2</sub>)<sub>r</sub>NR<sup>2d</sup>R<sup>2d</sup>, (CH<sub>2</sub>)<sub>r</sub>N(→O)R<sup>2d</sup>R<sup>2d</sup>, (CH<sub>2</sub>)<sub>r</sub>OR<sup>2d</sup>, (CH<sub>2</sub>)<sub>r</sub>-C(O)NR<sup>2d</sup>R<sup>2d</sup>, (CH<sub>2</sub>)<sub>r</sub>-NR<sup>2d</sup>C(O)R<sup>2e</sup>, (CH<sub>2</sub>)<sub>r</sub>-C(O)R<sup>2e</sup>, (CH<sub>2</sub>)<sub>r</sub>-NR<sup>2d</sup>C(O)NR<sup>2d</sup>R<sup>2d</sup>, (CH<sub>2</sub>)<sub>r</sub>-NR<sup>2d</sup>C(O)OR<sup>2d</sup>, (CH<sub>2</sub>)<sub>r</sub>-NR<sup>2d</sup>SO<sub>2</sub>R<sup>2d</sup>, and (CH<sub>2</sub>)<sub>r</sub>-S(O)<sub>p</sub>R<sup>2d</sup>, provided that S(O)<sub>p</sub>R<sup>2d</sup> forms other than S(O)<sub>2</sub>H or S(O)H;

15

R<sup>4b</sup>, at each occurrence, is selected from H, =O, OR<sup>3</sup>, CH<sub>2</sub>OR<sup>3</sup>, F, Cl, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, NR<sup>3</sup>R<sup>3a</sup>, CH<sub>2</sub>NR<sup>3</sup>R<sup>3a</sup>, C(O)R<sup>3</sup>, C(O)OR<sup>3c</sup>, NR<sup>3</sup>C(O)R<sup>3a</sup>, C(O)NR<sup>3</sup>R<sup>3a</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>3a</sup>, NR<sup>3</sup>SO<sub>2</sub>-phenyl, S(O)<sub>2</sub>CH<sub>3</sub>, S(O)<sub>2</sub>-phenyl, and CF<sub>3</sub>;

20

R<sup>4c</sup>, at each occurrence, is selected from =O, OH, OCH<sub>3</sub>, OCH<sub>2</sub>CH<sub>3</sub>, OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, OCH(CH<sub>3</sub>)<sub>2</sub>, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH(CH<sub>3</sub>)<sub>2</sub>, C<sub>2-3</sub> alkenyl, C<sub>2-3</sub> alkynyl, CH<sub>2</sub>OH, CH<sub>2</sub>OCH<sub>3</sub>, CH<sub>2</sub>OCH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>, CH<sub>2</sub>OCH(CH<sub>3</sub>)<sub>2</sub>, F, Br, Cl, CF<sub>3</sub>, NR<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, N(→O)R<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>N(→O)R<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2c</sup>, CH<sub>2</sub>C(O)R<sup>2c</sup>, NR<sup>2</sup>C(O)R<sup>2b</sup>, CH<sub>2</sub>NR<sup>2</sup>C(O)R<sup>2b</sup>, C(O)NR<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>C(O)NR<sup>2</sup>R<sup>2a</sup>, SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, NR<sup>2</sup>SO<sub>2</sub>R<sup>5a</sup>, CH<sub>2</sub>NR<sup>2</sup>SO<sub>2</sub>R<sup>5a</sup>, S(O)<sub>p</sub>R<sup>5a</sup>, CH<sub>2</sub>S(O)<sub>p</sub>R<sup>5a</sup>, CF<sub>3</sub>, cyclopropyl substituted with 0-1 R<sup>4b</sup>, cyclobutyl substituted with 0-1 R<sup>4b</sup>, cyclopentyl substituted with 0-1 R<sup>4b</sup>, phenyl substituted with 0-1 R<sup>4b</sup>, -CH<sub>2</sub>-cyclopropyl substituted

25

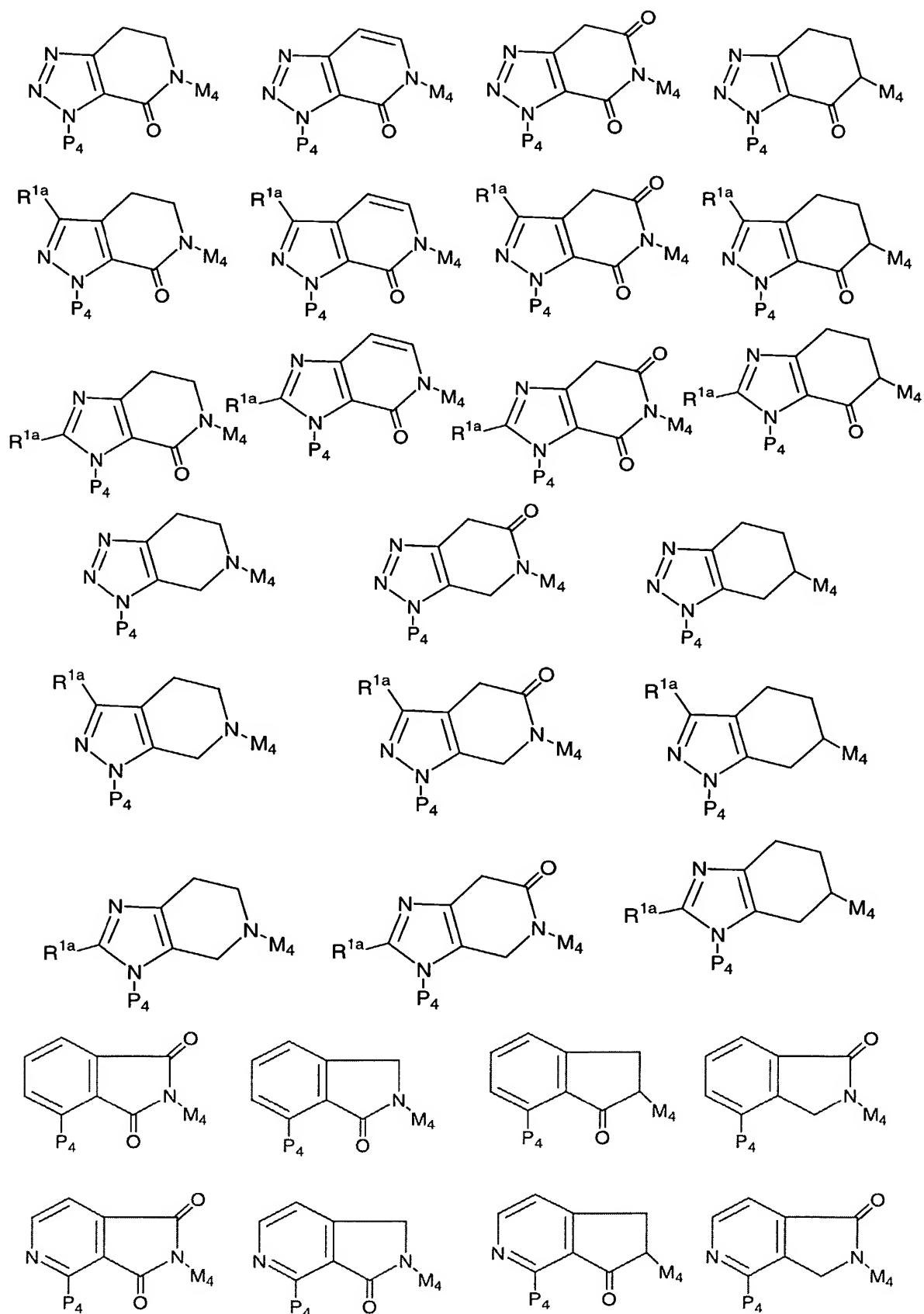
30

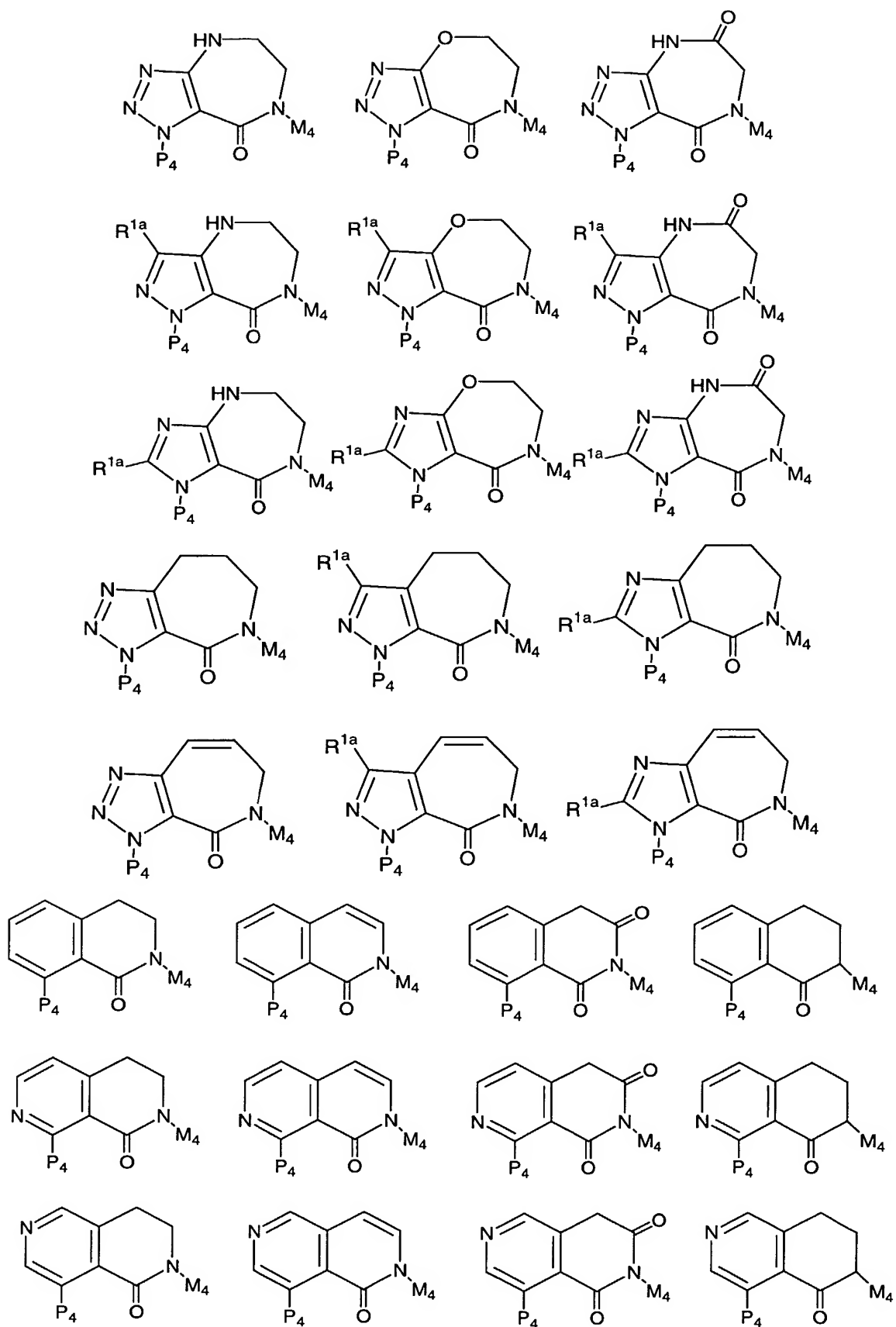
with 0-1 R<sup>4b</sup>, -CH<sub>2</sub>-cyclobutyl substituted with 0-1 R<sup>4b</sup>,  
-CH<sub>2</sub>-cyclopentyl substituted with 0-1 R<sup>4b</sup>, benzyl  
substituted with 0-2 R<sup>4b</sup>, 5-6 membered aromatic  
heterocycle substituted with 0-2 R<sup>4b</sup> and consisting of  
5 carbon atoms and from 1-4 heteroatoms selected from  
the group consisting of N, O, and S(O)<sub>p</sub>, and (CH<sub>2</sub>)<sub>5-6</sub>  
membered aromatic heterocycle substituted with 0-2 R<sup>4b</sup>  
and consisting of carbon atoms and from 1-4  
heteroatoms selected from the group consisting of N,  
10 O, and S(O)<sub>p</sub>;

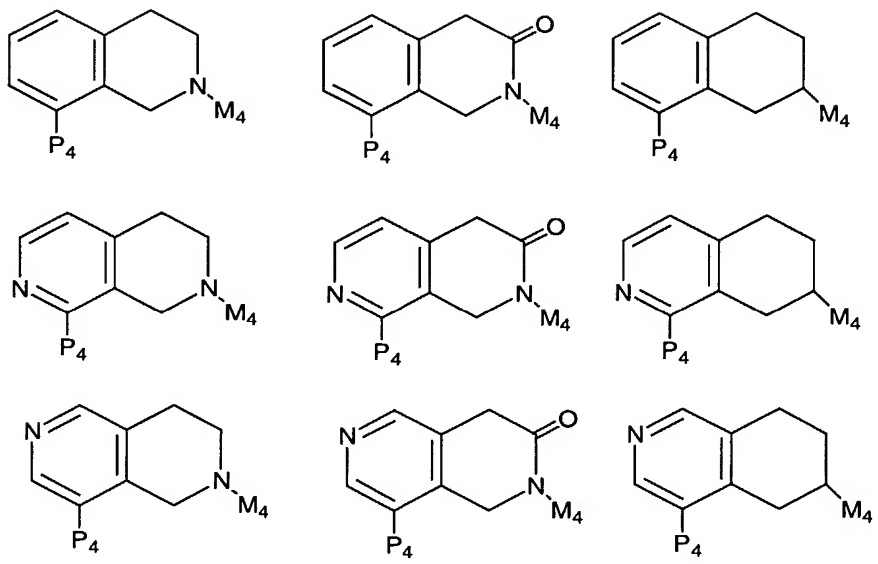
R<sup>5</sup>, at each occurrence, is selected from H, =O, CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>,  
OR<sup>3</sup>, CH<sub>2</sub>OR<sup>3</sup>, F, Cl, NR<sup>3</sup>R<sup>3a</sup>, CH<sub>2</sub>NR<sup>3</sup>R<sup>3a</sup>, C(O)R<sup>3</sup>, C(O)OR<sup>3c</sup>,  
NR<sup>3</sup>C(O)R<sup>3a</sup>, C(O)NR<sup>3</sup>R<sup>3a</sup>, SO<sub>2</sub>NR<sup>3</sup>R<sup>3a</sup>, NR<sup>3</sup>SO<sub>2</sub>-C<sub>1-4</sub> alkyl,  
15 NR<sup>3</sup>SO<sub>2</sub>-phenyl, S(O)<sub>2</sub>-CH<sub>3</sub>, S(O)<sub>2</sub>-phenyl, CF<sub>3</sub>, phenyl  
substituted with 0-2 R<sup>6</sup>, naphthyl substituted with 0-2  
R<sup>6</sup>, and benzyl substituted with 0-2 R<sup>6</sup>; and,

R<sup>6</sup>, at each occurrence, is selected from H, OH, OR<sup>2</sup>, F, Cl,  
20 CH<sub>3</sub>, CH<sub>2</sub>CH<sub>3</sub>, NR<sup>2</sup>R<sup>2a</sup>, CH<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>, C(O)R<sup>2b</sup>, CH<sub>2</sub>C(O)R<sup>2b</sup>,  
NR<sup>2</sup>C(O)R<sup>2b</sup>, and SO<sub>2</sub>NR<sup>2</sup>R<sup>2a</sup>.

[6] In another preferred embodiment, the present invention  
25 provides a novel compound, wherein the compound is selected  
from:





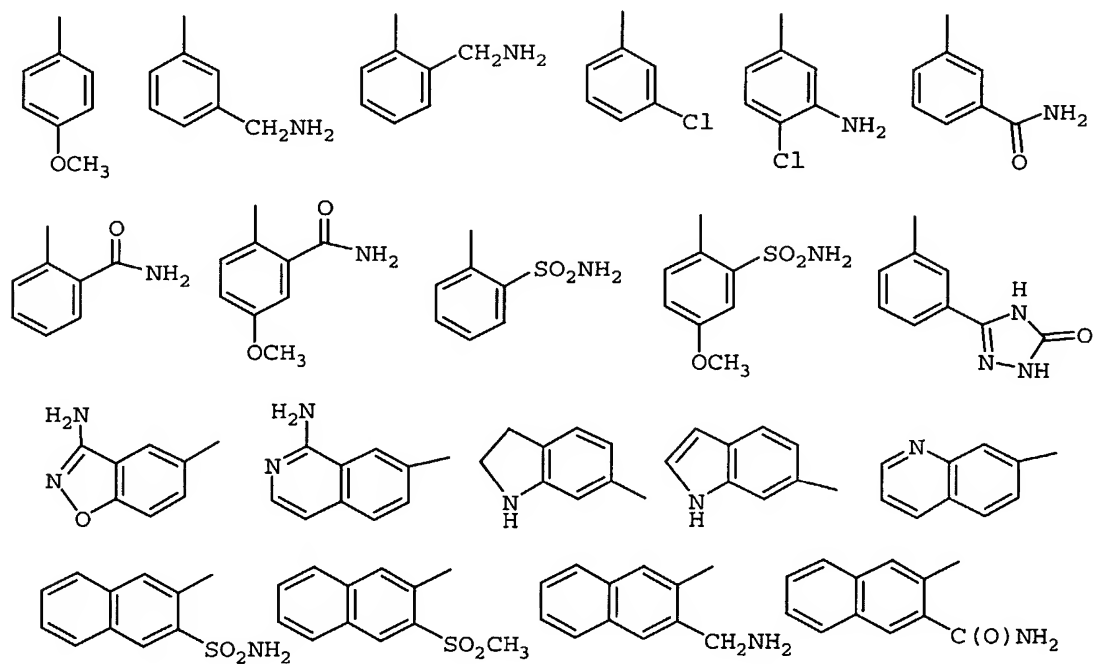


$P_4$  is  $-G_1-G$ ;

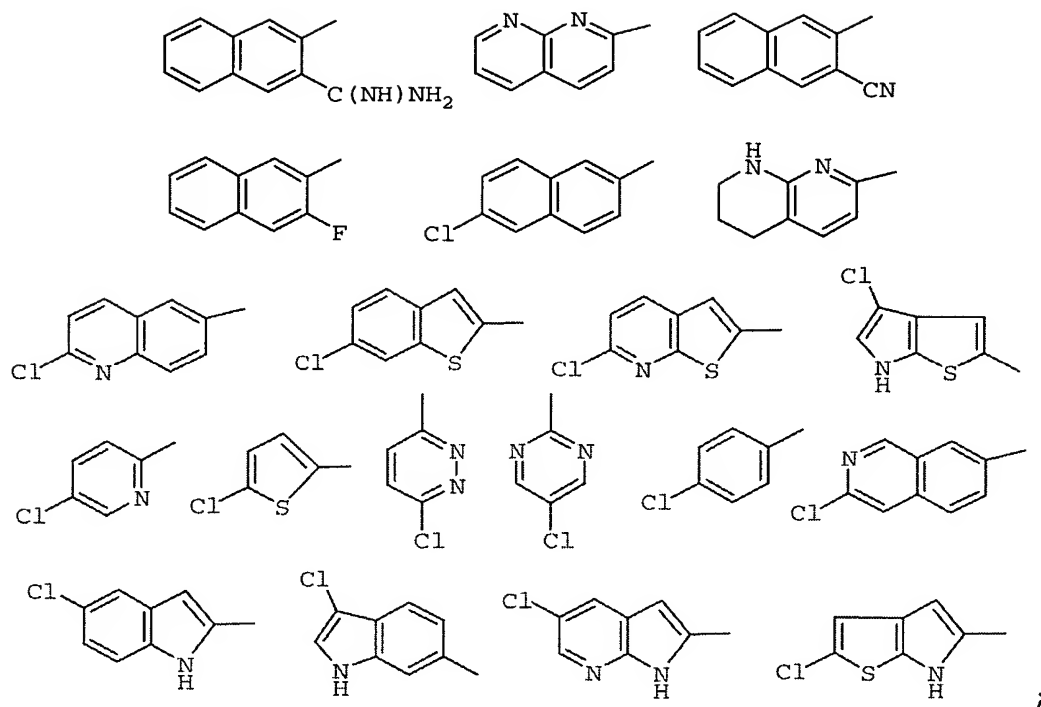
5

$M_4$  is  $-A-B$ ;

$-G$  is selected from:



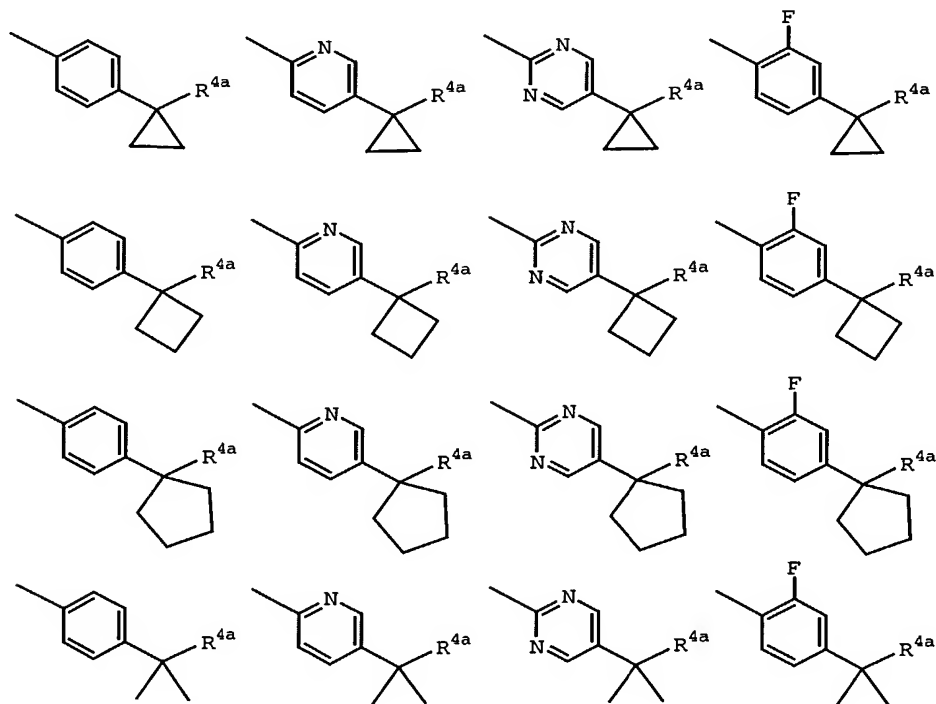
10

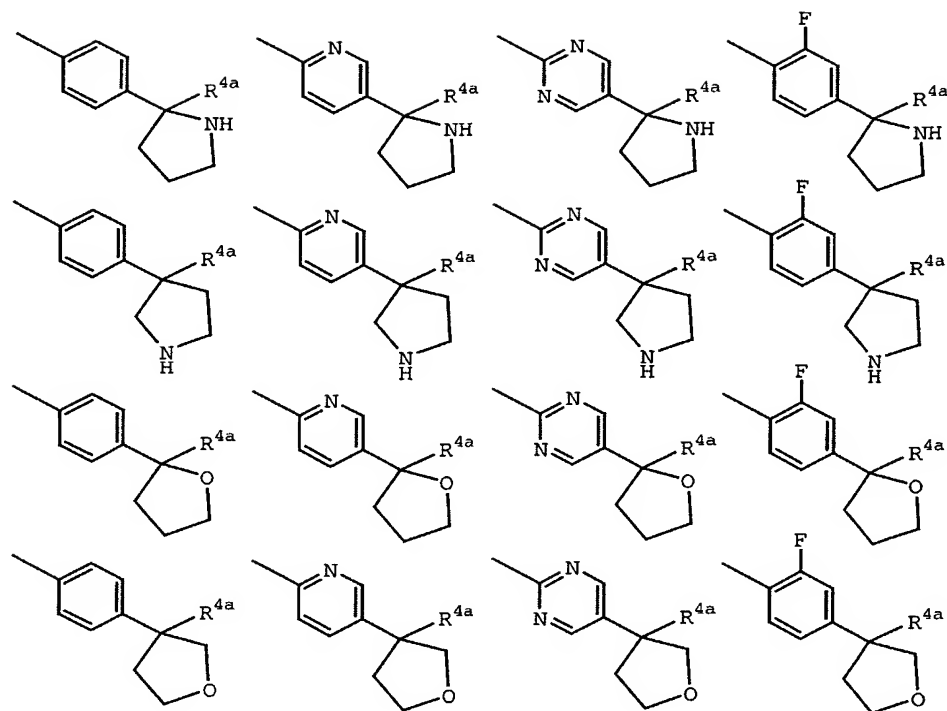


$G_1$  is absent or is selected from  $C(O)NH$ ,  $NHC(O)$ , and  $NHSO_2$ ;

5

A-B is selected from:





Z is selected from a bond, CH<sub>2</sub>, and CH<sub>2</sub>CH<sub>2</sub>;

- 5 R<sup>2d</sup>, at each occurrence, is selected from H, C<sub>1-4</sub> alkyl substituted with 0-1 R<sup>4c</sup>, C<sub>3-6</sub> cycloalkyl substituted with 0-2 R<sup>4c</sup>, phenyl substituted with 0-2 R<sup>4c</sup>, and a 5-6 membered aromatic heterocycle consisting of:
- 10 carbon atoms and 1-4 heteroatoms selected from the group consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2d</sup> forms other than a N-halo, N-C-halo, S(O)<sub>p</sub>-halo, O-halo, N-S, S-N, S(O)<sub>p</sub>-S(O)<sub>p</sub>, S-O, O-N, O-S, or O-O moiety;
- 15 R<sup>2e</sup>, at each occurrence, is selected from H, C<sub>1-4</sub> alkyl substituted with 0-1 R<sup>4c</sup>, C<sub>3-6</sub> cycloalkyl substituted with 0-2 R<sup>4c</sup>, phenyl, substituted with 0-2 R<sup>4c</sup>, and 5-6 membered aromatic heterocycle consisting of: carbon atoms and 1-4 heteroatoms selected from the group
- 20 consisting of N, O, and S(O)<sub>p</sub>, provided that R<sup>2e</sup> forms other than a C(O)-halo or C(O)-S(O)<sub>p</sub> moiety;

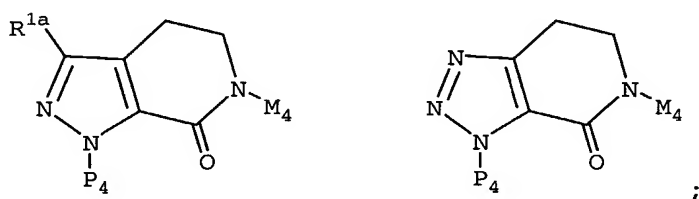
$R^{4a}$  is selected from  $NR^{2d}R^{2d}$ ,  $CH_2NR^{2d}R^{2d}$ ,  $CH_2CH_2NR^{2d}R^{2d}$ ,  
 $N(\rightarrow O)R^{2d}R^{2d}$ ,  $CH_2N(\rightarrow O)R^{2d}R^{2d}$ ,  $CH_2OR^{2d}$ ,  $C(O)R^{2e}$ ,  
 $C(O)NR^{2d}R^{2d}$ ,  $CH_2C(O)NR^{2d}R^{2d}$ ,  $NR^{2d}C(O)R^{2e}$ ,  $CH_2NR^{2d}C(O)R^{2e}$ ,  
5  $NR^{2d}C(O)NR^{2d}R^{2d}$ ,  $CH_2NR^{2d}C(O)NR^{2d}R^{2d}$ ,  $NR^{2d}C(O)OR^{2d}$ ,  
 $CH_2NR^{2d}C(O)OR^{2d}$ ,  $NR^{2d}SO_2R^{2d}$ ,  $CH_2NR^{2d}SO_2R^{2d}$ ,  $S(O)_pR^{2d}$ ,  
 $CH_2S(O)_pR^{2d}$ , 5-6 membered carbocycle substituted with  
0-2  $R^{4c}$ ,  $-(CH_2)$ -5-6 membered carbocycle substituted  
with 0-2  $R^{4c}$ ,  $-(CH_2)_2$ -5-6 membered carbocycle  
10 substituted with 0-2  $R^{4c}$ , 5-6 membered heterocycle  
substituted with 0-2  $R^{4c}$  and consisting of: carbon  
atoms and 1-4 heteroatoms selected from the group  
consisting of N, O, and  $S(O)_p$ ,  $-(CH_2)$ -5-6 membered  
heterocycle substituted with 0-2  $R^{4c}$  and consisting of:  
15 carbon atoms and 1-4 heteroatoms selected from the  
group consisting of N, O, and  $S(O)_p$ , and  $-(CH_2)_2$ -5-6  
membered heterocycle substituted with 0-2  $R^{4c}$  and  
consisting of: carbon atoms and 1-4 heteroatoms  
selected from the group consisting of N, O, and  $S(O)_p$   
20 provided that  $S(O)_pR^{2d}$  forms other than  $S(O)_2H$  or  
 $S(O)H$ ; and,

$R^{4c}$  is selected from  $=O$ ,  $OH$ ,  $OCH_3$ ,  $OCH_2CH_3$ ,  $OCH_2CH_2CH_3$ ,  
 $OCH(CH_3)_2$ ,  $CH_3$ ,  $CH_2CH_3$ ,  $CH_2CH_2CH_3$ ,  $CH(CH_3)_2$ ,  $CH=CH_2$ ,  
25  $CH\equiv CH$ ,  $CH_2OH$ ,  $CH_2OCH_3$ ,  $CH_2OCH_2CH_3$ ,  $CH_2OCH_2CH_2CH_3$ ,  
 $CH_2OCH(CH_3)_2$ ,  $F$ ,  $Br$ ,  $Cl$ ,  $CF_3$ ,  $NR^{2a}R^{2a}$ ,  $CH_2NR^{2a}R^{2a}$ ,  
 $C(O)R^{2c}$ ,  $CH_2C(O)R^{2c}$ ,  $NR^{2a}C(O)R^{2b}$ ,  $CH_2NR^{2a}C(O)R^{2b}$ ,  
 $C(O)NR^{2a}R^{2a}$ ,  $CH_2C(O)NR^{2a}R^{2a}$ ,  $SO_2NR^{2a}R^{2a}$ ,  $CH_2SO_2NR^{2a}R^{2a}$ ,  
 $NR^{2a}SO_2R^{5a}$ ,  $CH_2NR^{2a}SO_2R^{5a}$ ,  $S(O)_pR^{5a}$ , and  $CH_2S(O)_pR^{5a}$ .

30



[7] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is selected from:

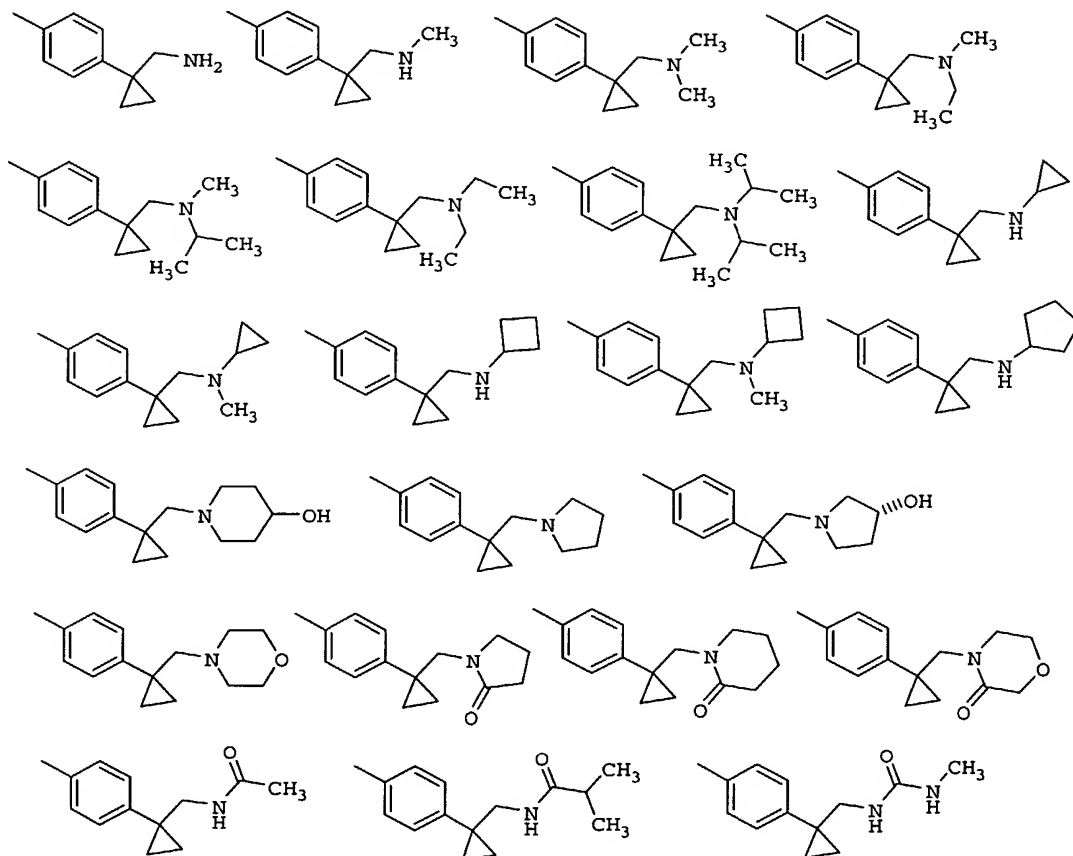


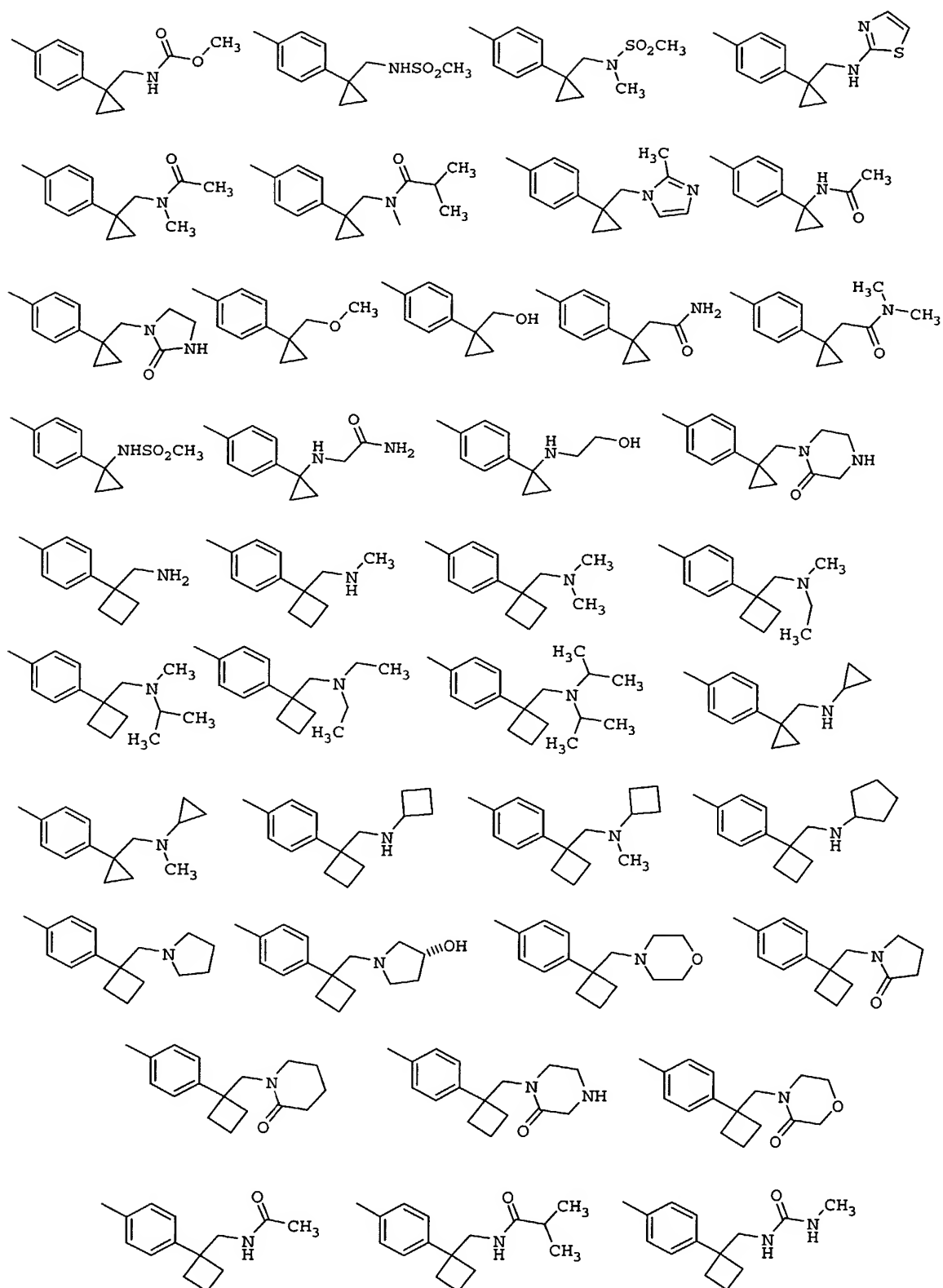
5  $P_4$  is -G;

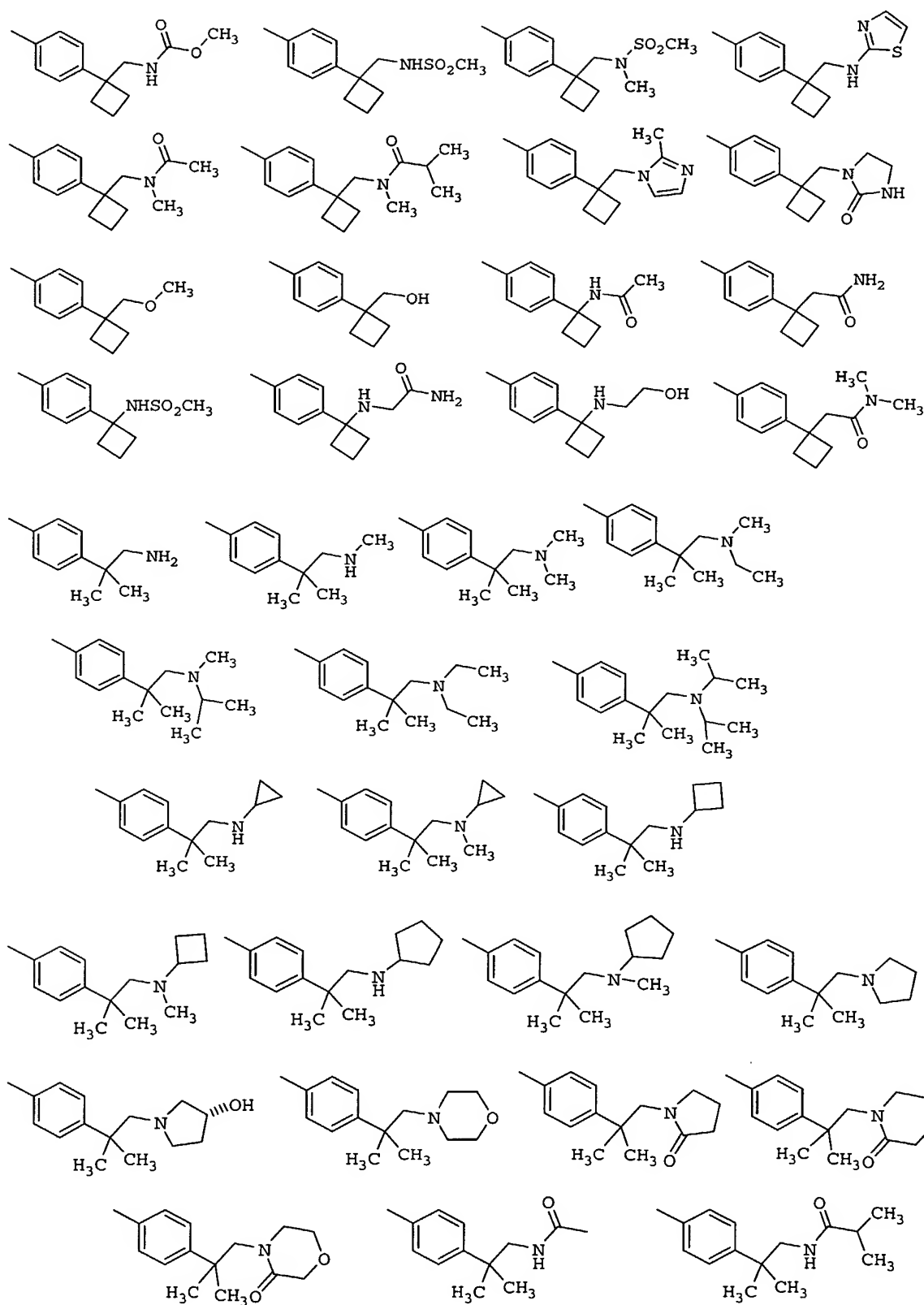
$M_4$  is -A-B;

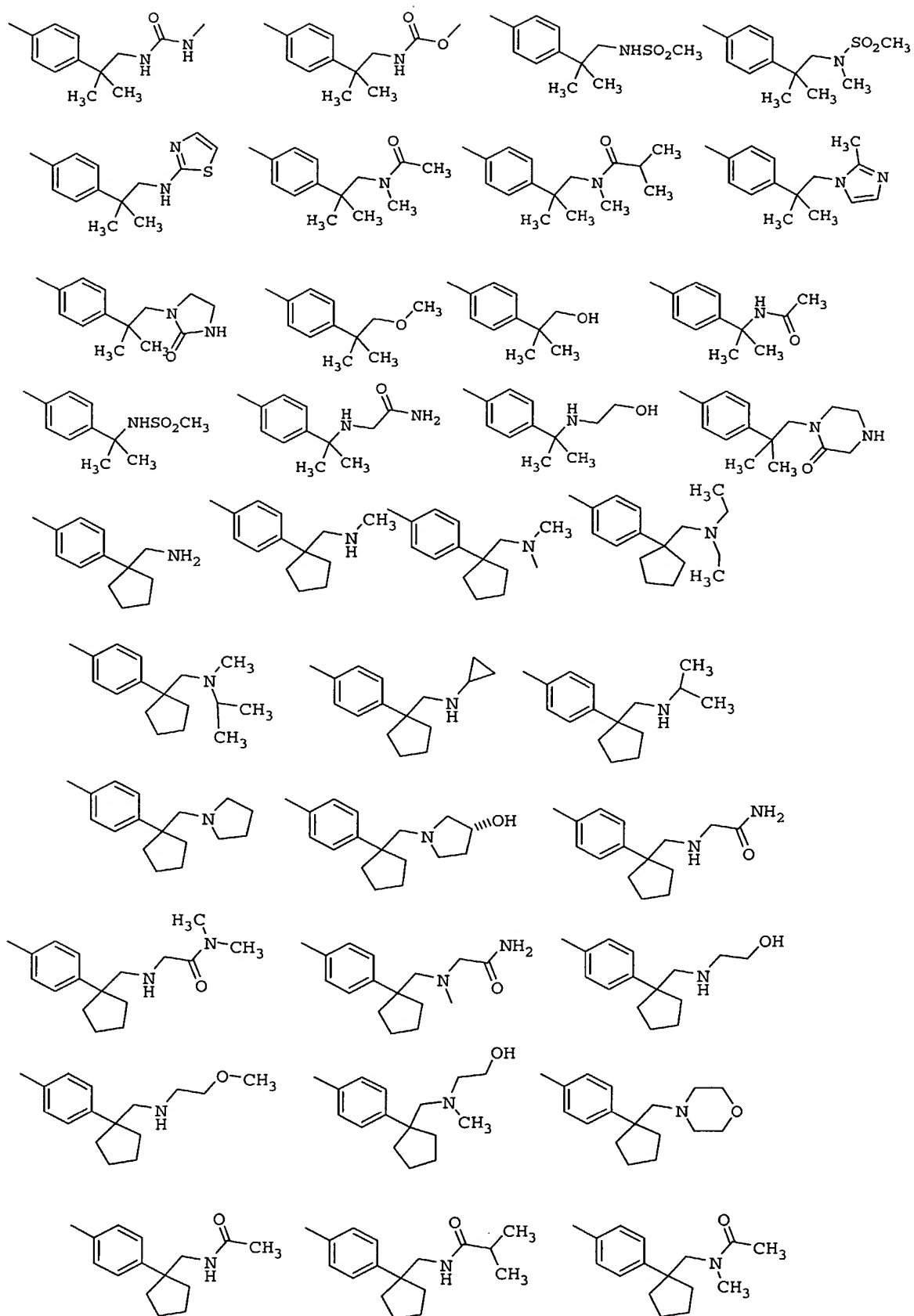
A-B is selected from:

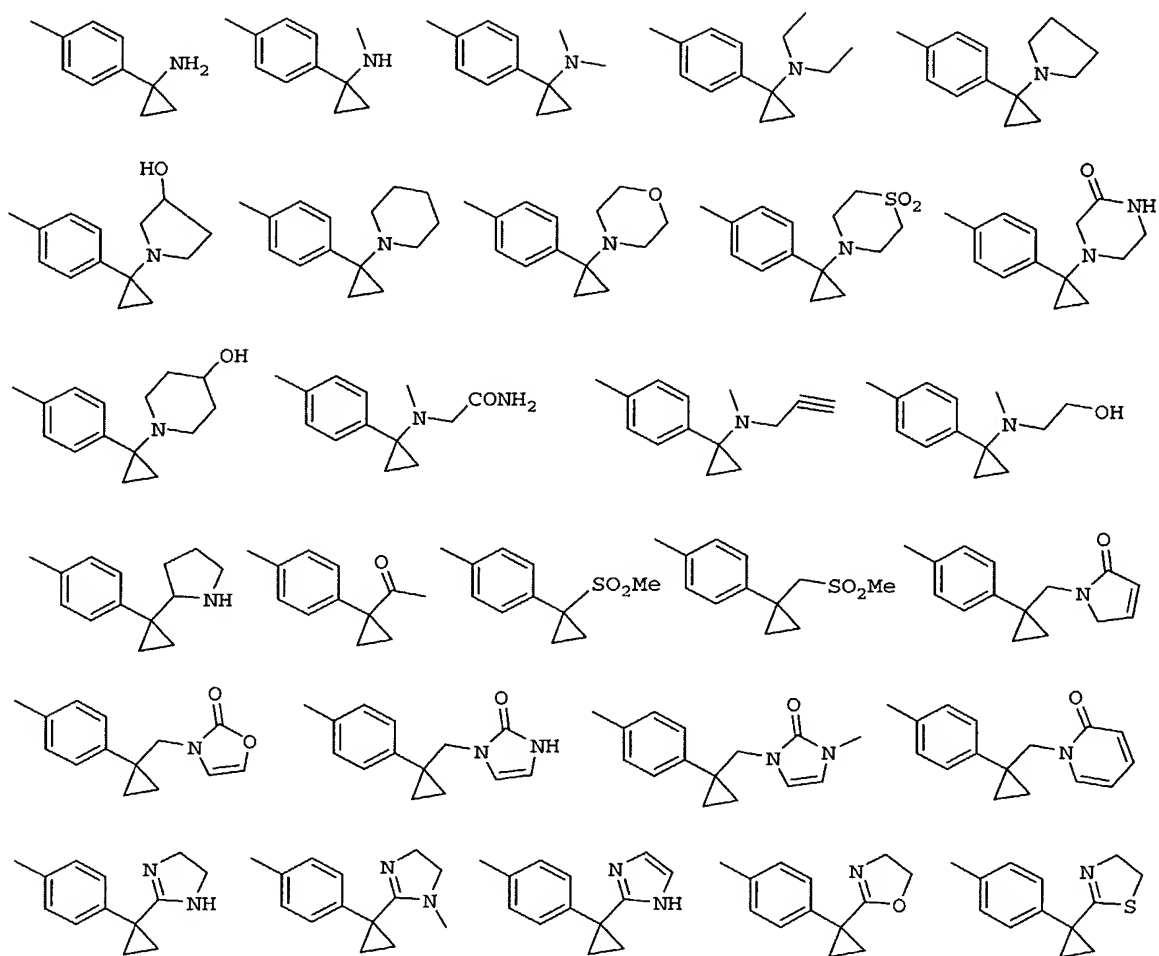
10

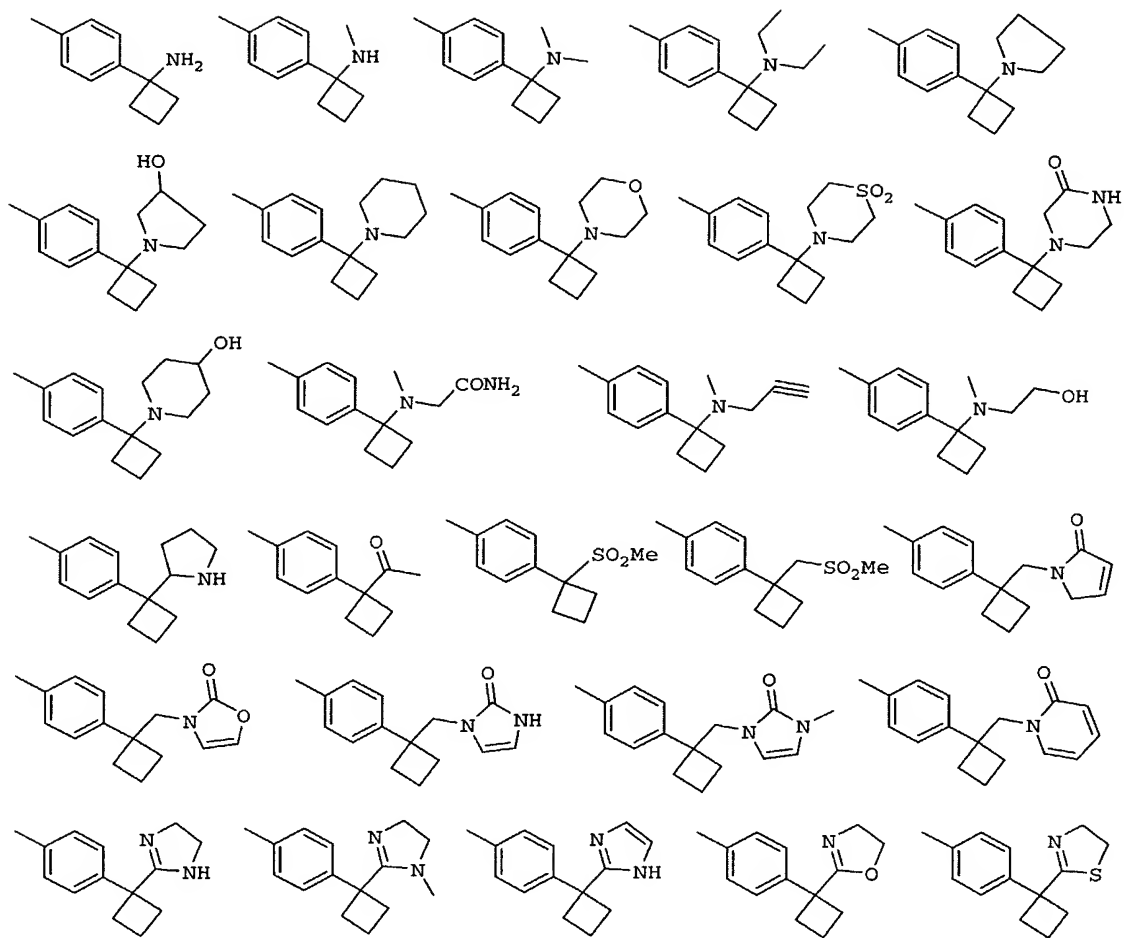


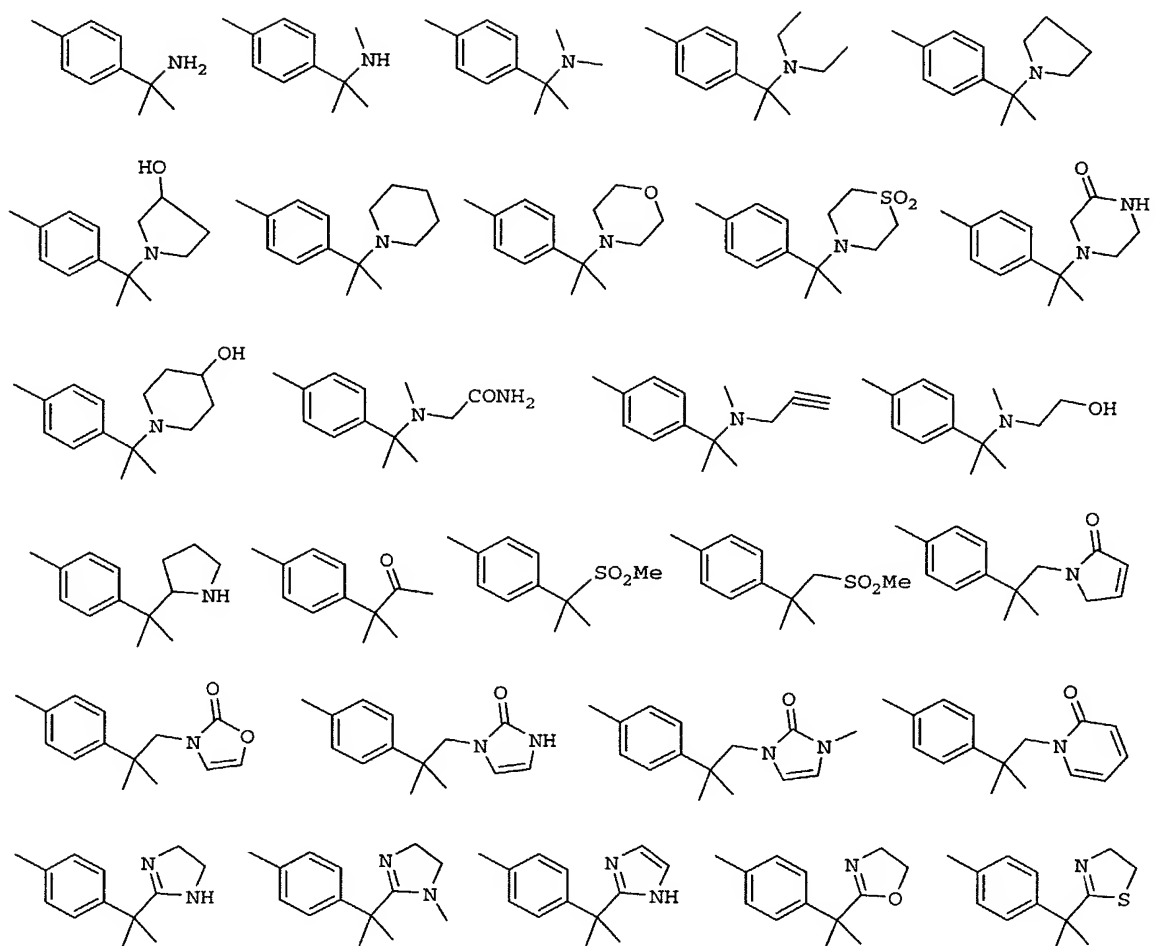


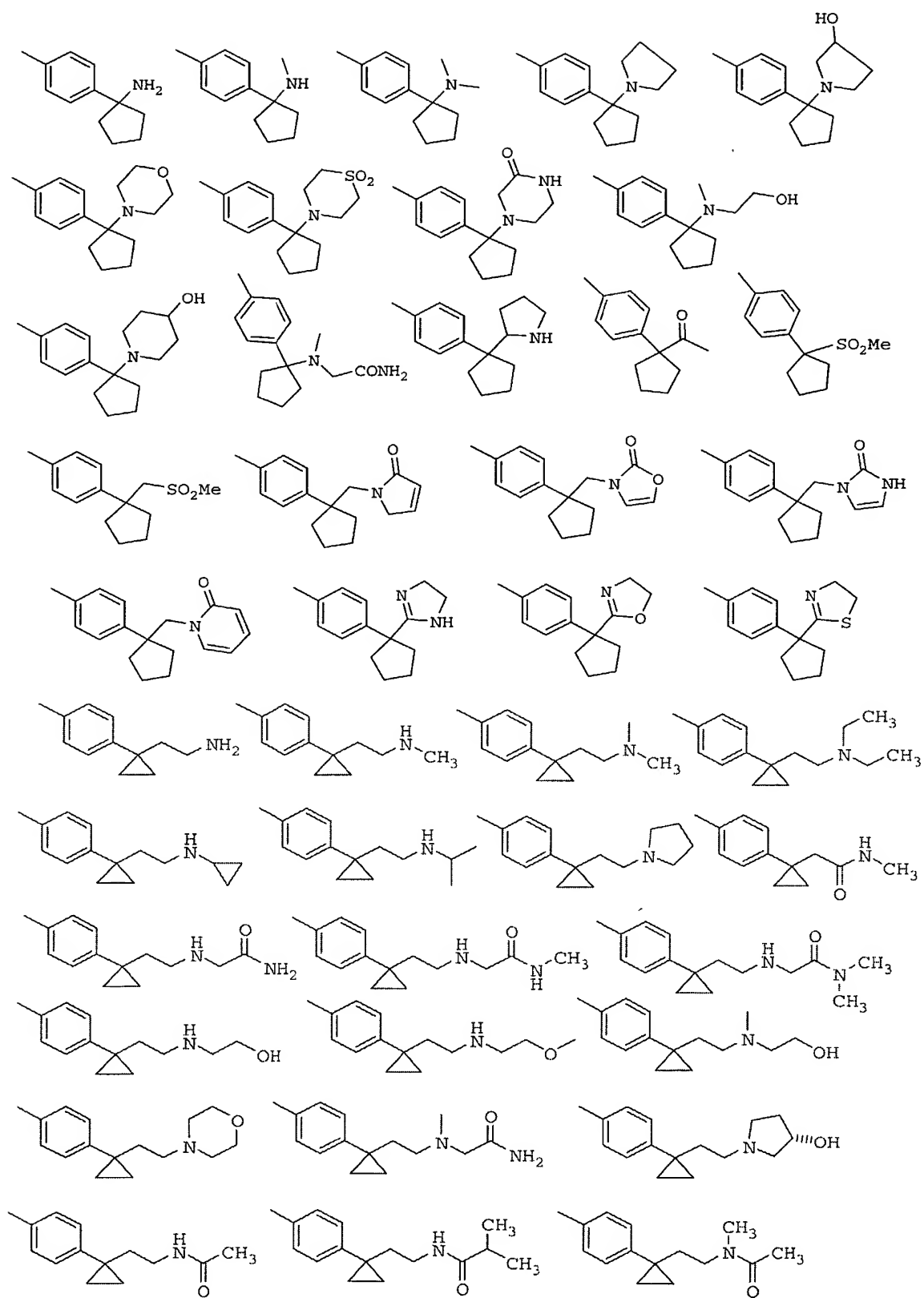




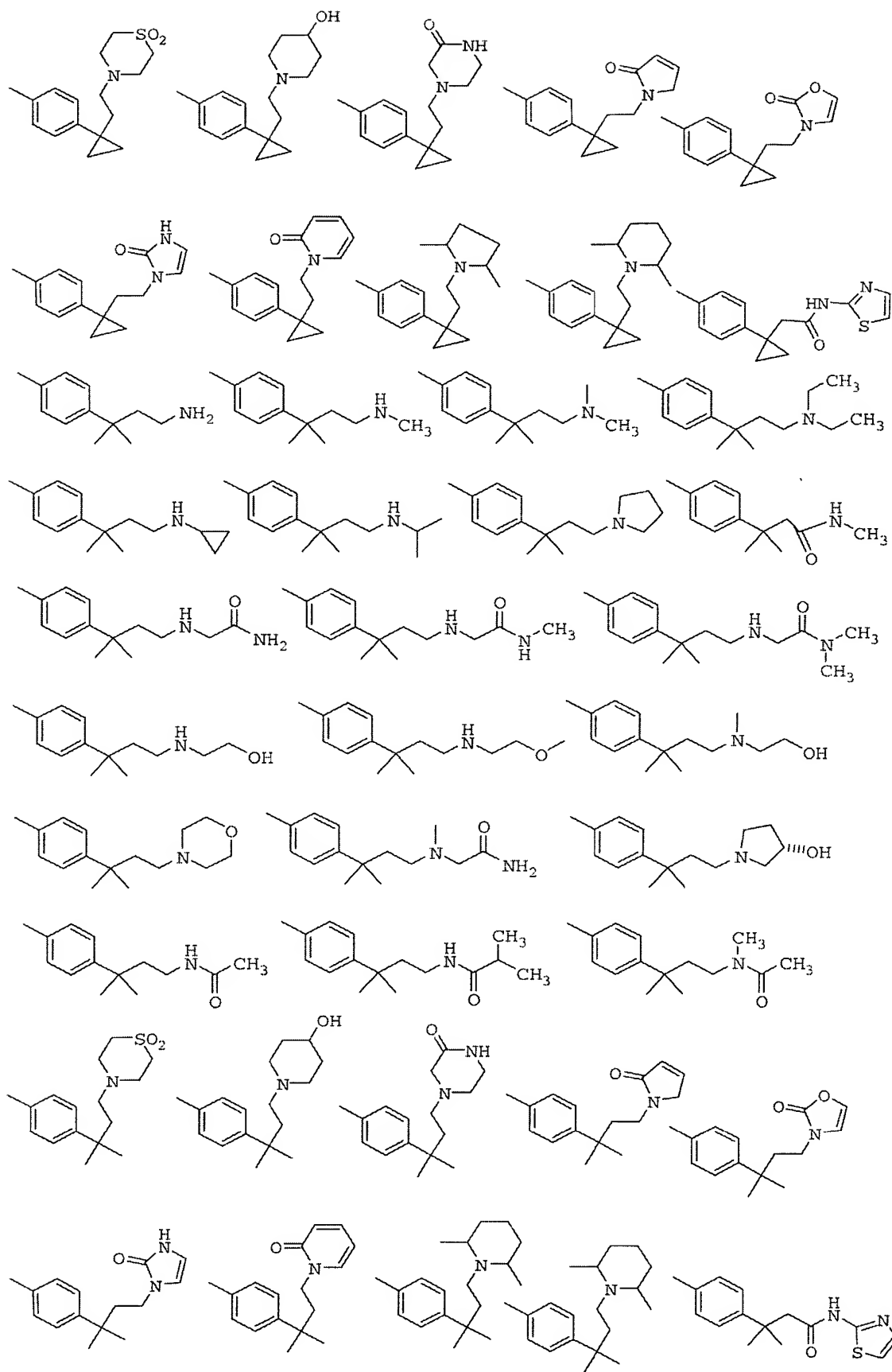


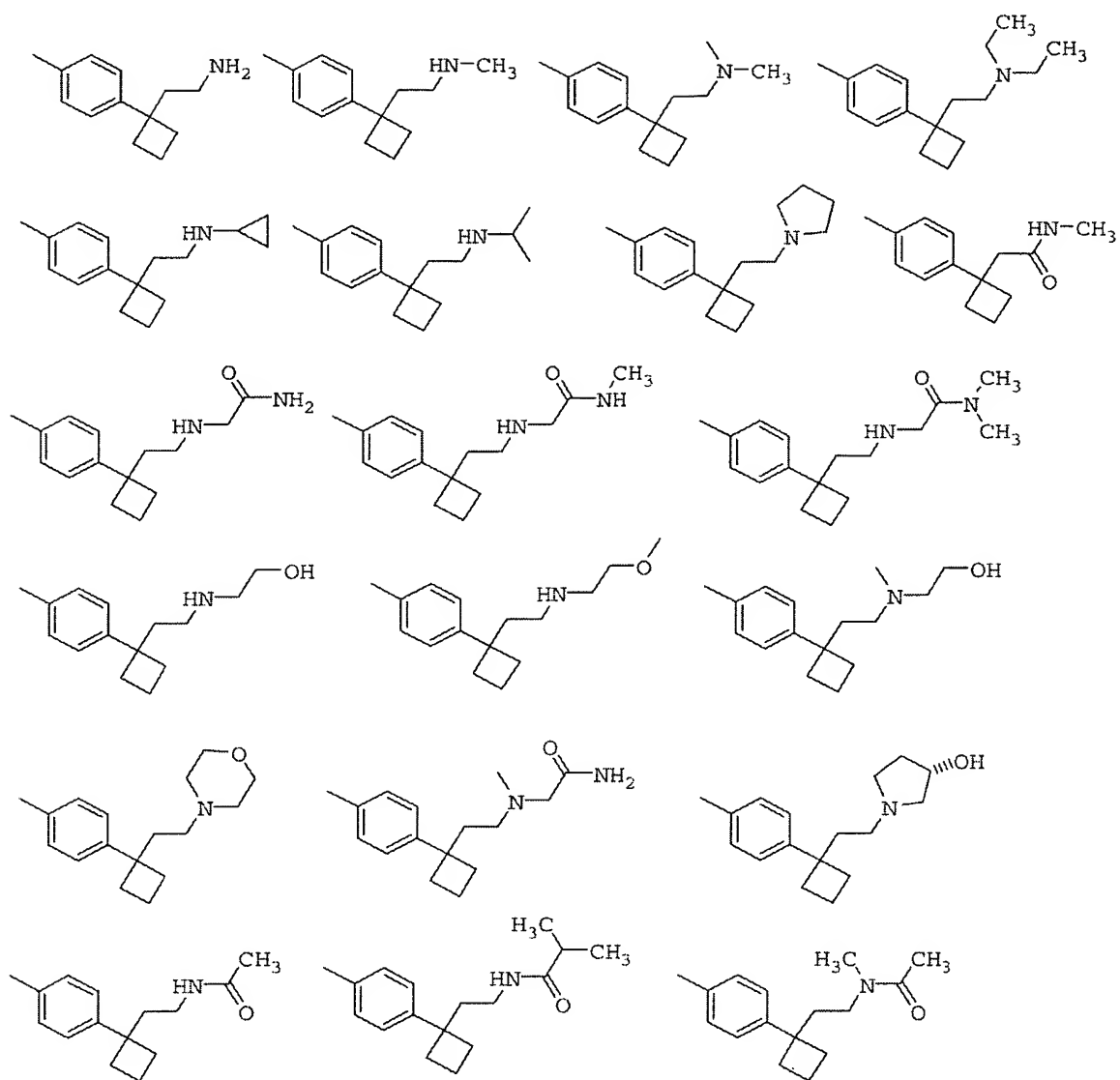


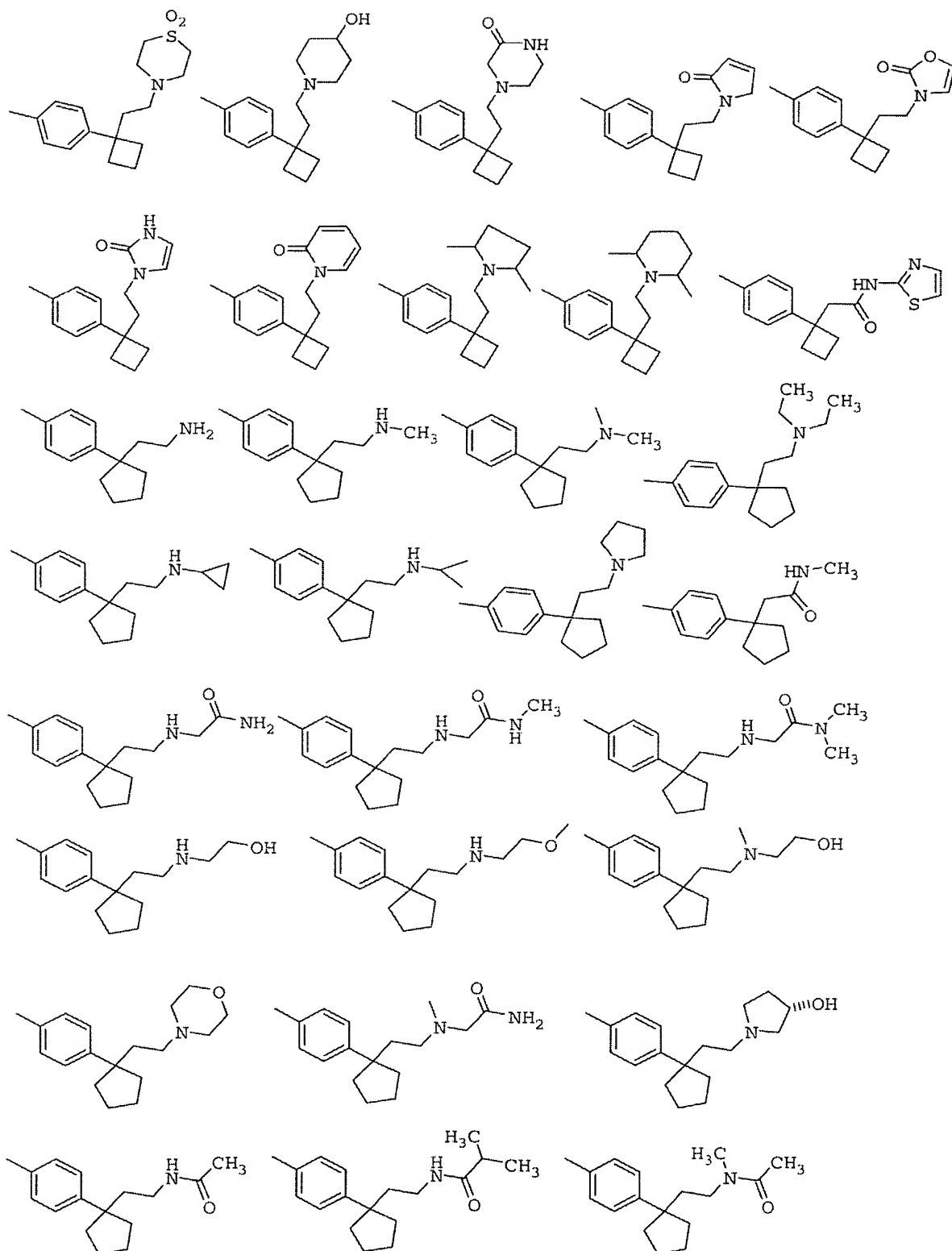


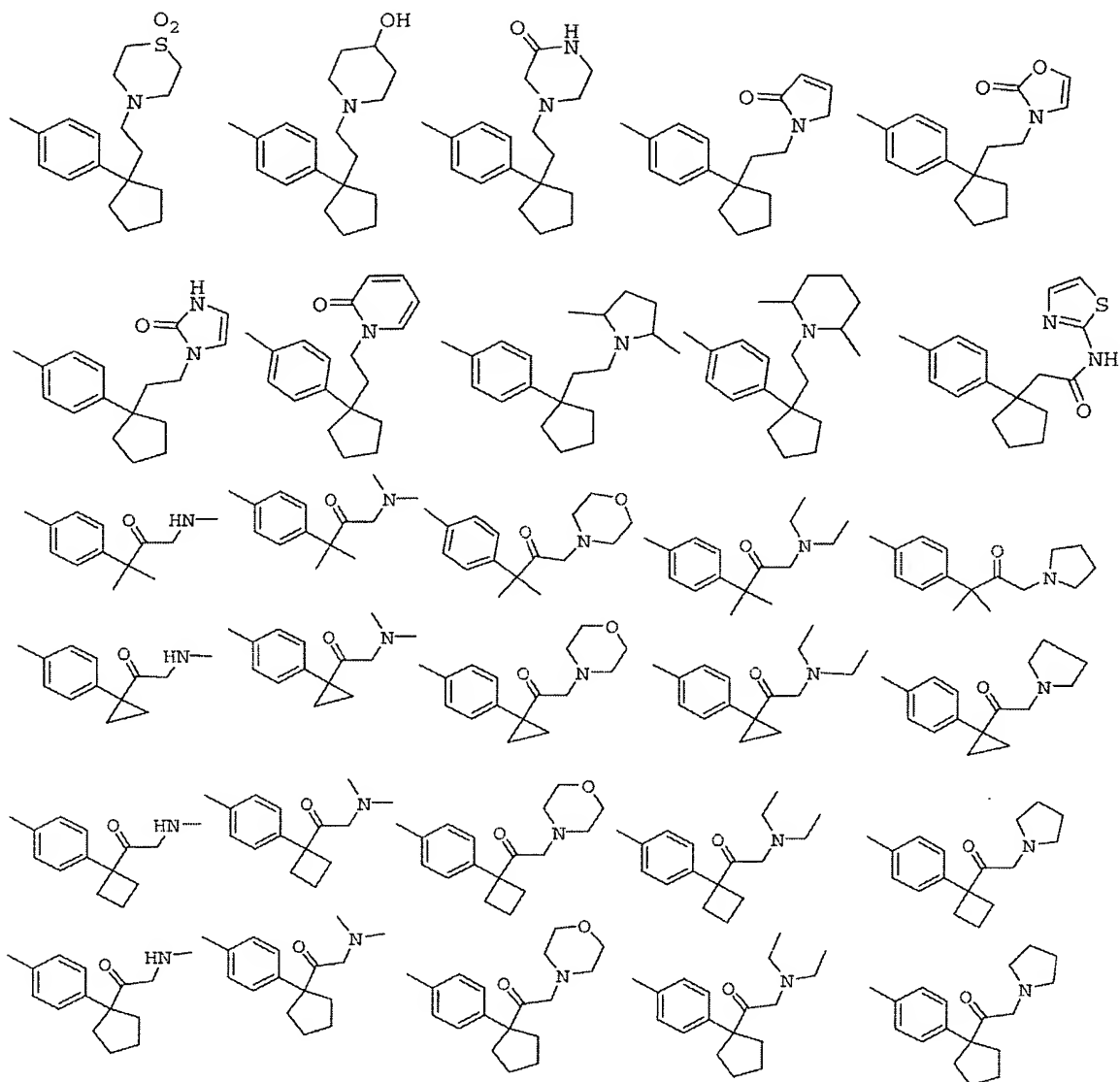












- 5 [8] In another preferred embodiment, the present invention provides a novel compound, wherein the compound is selected from the group:

10 1-(4-methoxyphenyl)-6-(4-{1-  
 [(methylamino)methyl]cyclopropyl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

- 6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 5 6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 10 6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 15 6-(4-{1-[(cyclopentylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 20 1-(4-methoxyphenyl)-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 25 6-[4-(1-{[(3R)-3-hydroxy-1-pyrrolidinyl]methyl}cyclopropyl)phenyl]-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 30 6-(4-{1-[(4-hydroxy-1-piperidinyl)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 35 1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

- 1-(4-methoxyphenyl)-6-{4-[1-(1-pyrrolidinylcarbonyl)cyclopropyl]phenyl}-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 5 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}-N,N-dimethylcyclopropanecarboxamide;
- 10 1-(4-methoxyphenyl)-6-(4-{1-[(4-methyl-1-piperazinyl)carbonyl]cyclopropyl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 15 6-{4-[1-(4-hydroxypiperidine-1-carbonyl)cyclopropyl]phenyl}-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 20 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropanecarboxamide;
- 25 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropanecarboxylic acid  
cyclopentylamide;
- 30 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}-N-(1,3,4-thiadiazol-2-yl)cyclopropanecarboxamide;
- 35 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-

yl}phenyl}-N-(1*H*-tetraazol-5-  
yl)cyclopropanecarboxamide;

5 methyl 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-  
yl}phenyl}cyclopropanecarboxylate;

10 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-  
yl}phenyl}cyclopropanecarbonitrile;

15 6-{4-[1-(aminomethyl)cyclopropyl]phenyl}-1-(4-  
methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-  
7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

*N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-  
yl}phenyl}cyclopropyl)methyl]-*N*-methylacetamide;

20 *N*'-ethyl-*N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-  
(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-  
*c*]pyridin-6-yl}phenyl}cyclopropyl)methyl]-*N*-  
methylurea;

25 *N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-  
yl}phenyl}cyclopropyl)methyl]-*N*-  
methylmethanesulfonamide;

30 1-(4-methoxyphenyl)-6-{4-[1-(2-methylimidazol-1-  
ylmethyl)cyclopropyl]phenyl}-3-trifluoromethyl-  
1,4,5,6-tetrahydro-pyrazolo[3,4-*c*]pyridin-7-one;

35 1-(4-methoxyphenyl)-6-{4-[1-(thiazol-2-ylaminomethyl)-  
cyclopropyl]phenyl}-3-trifluoromethyl-1,4,5,6-  
tetrahydro-pyrazolo[3,4-*c*]pyridin-7-one;

methyl 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-  
yl]phenyl}cyclopentanecarboxylate;

5

1-(4-methoxyphenyl)-6-(4-{1-  
[(methylamino)methyl]cyclopentyl}phenyl)-3-  
(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-  
*c*]pyridin-7-one;

10

6-(4-{1-[(dimethylamino)methyl]cyclopentyl}phenyl)-1-(4-  
methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-  
7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

15

1-(4-methoxyphenyl)-6-{4-[1-(1-  
pyrrolidinylmethyl)cyclopentyl]phenyl}-3-  
(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-  
*c*]pyridin-7-one;

20

6-[4-(1-{[(3*R*)-3-hydroxy-1-  
pyrrolidinyl]methyl}cyclopentyl)phenyl]-1-(4-  
methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-  
7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

25

1-(4-methoxyphenyl)-6-{4-[1-(4-  
morpholinylmethyl)cyclopentyl]phenyl}-3-  
(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-  
*c*]pyridin-7-one;

30

*N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-  
yl]phenyl}cyclopentyl)methyl]-*N*-methylacetamide;

35

*N*-[(1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-



yl]phenyl)cyclopentyl)methyl]-N-  
methylemethanesulfonamide;

5 methyl 1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-  
1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-  
yl]phenyl)cyclobutanecarboxylate;

1-(4-methoxyphenyl)-6-(4-{1-  
[(methylamino)methyl]cyclobutyl}phenyl)-3-  
10 (trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-  
c]pyridin-7-one;

6-(4-{1-[(dimethylamino)methyl]cyclobutyl}phenyl)-1-(4-  
methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-  
15 7H-pyrazolo[3,4-c]pyridin-7-one;

6-(4-{1-[(diethylamino)methyl]cyclobutyl}phenyl)-1-(4-  
methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-  
20 7H-pyrazolo[3,4-c]pyridin-7-one;

1-(4-methoxyphenyl)-6-{4-[1-(1-  
pyrrolidinylmethyl)cyclobutyl]phenyl}-3-  
(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-  
c]pyridin-7-one;

25 6-[4-(1-{[(3R)-3-hydroxy-1-  
pyrrolidinyl]methyl}cyclobutyl)phenyl]-1-(4-  
methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-  
7H-pyrazolo[3,4-c]pyridin-7-one;

30 1-(4-methoxyphenyl)-6-{4-[1-(4-  
morpholinylmethyl)cyclobutyl]phenyl}-3-  
(trifluoromethyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-  
c]pyridin-7-one;

35

- N*-[ (1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclobutyl)methyl]-*N*-methylacetamide;
- 5    *N*-[ (1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclobutyl)methyl]-*N*-methylmethanesulfonamide;
- 10    1-{4-[1-(4-Methoxyphenyl)-7-oxo-3-trifluoromethyl-1,4,5,7-tetrahydro-pyrazolo[3,4-*c*]pyridin-6-yl]-phenyl}cyclohexanecarboxylic acid methyl ester;
- 15    1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclohexyl}phenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;
- 20    6-(4-{1-[(dimethylamino)methyl]cyclohexyl}phenyl)-1-(4-methoxyphenyl)-3-(trifluoromethyl)-1,4,5,6-tetrahydro-7*H*-pyrazolo[3,4-*c*]pyridin-7-one;
- 25    *N*-[ (1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclohexyl)methyl]-*N*-methylacetamide;
- 30    *N*-[ (1-{4-[1-(4-methoxyphenyl)-7-oxo-3-(trifluoromethyl)-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclohexyl)methyl]-*N*-methylmethanesulfonamide;
- 35    1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro 7*H*-pyrazolo[3,4-*c*]pyridin-7-one;

- 6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methanesulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 5 6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methanesulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 10 6-(4-{1-[(cyclopentylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methanesulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 15 1-(4-methoxyphenyl)-3-(methanesulfonyl)-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 20 6-[4-(1-{[(3R)-3-hydroxy-1-pyrrolidinyl]methyl}cyclopropyl)phenyl]-1-(4-methoxyphenyl)-3-(methanesulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 25 6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-3-(methanesulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;
- 30 N-[(1-{4-[1-(4-methoxyphenyl)-3-(methanesulfonyl)-7-oxo-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropyl)methyl]-N-methylacetamide;
- 35 3-methanesulfonyl-1-(4-methoxyphenyl)-6-{4-[1-(2-methylimidazol-1-ylmethyl)cyclopropyl]phenyl}-1,4,5,6-tetrahydro-pyrazolo[3,4-c]pyridin-7-one;

3-methanesulfonyl-1-(4-methoxyphenyl)-6-{4-[1-(thiazol-2-ylaminomethyl)cyclopropyl]phenyl}-1,4,5,6-tetrahydro-pyrazolo[3,4-c]pyridin-7-one;

5

1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclobutyl}phenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro 7H-pyrazolo[3,4-c]pyridin-7-one;

10

6-(4-{1-[(dimethylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

15 6-(4-{1-[(isopropylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

1-(4-methoxyphenyl)-3-(methylsulfonyl)-6-{4-[1-(1-pyrrolidinylmethyl)cyclobutyl]phenyl}-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

20

6-[4-(1-{[(3R)-3-hydroxy-1-pyrrolidinyl]methyl}cyclobutyl)phenyl]-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

25

6-(4-{1-[(diethylamino)methyl]cyclobutyl}phenyl)-1-(4-methoxyphenyl)-3-(methylsulfonyl)-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

30

1-(4-methoxyphenyl)-3-(methylsulfonyl)-6-{4-[1-(4-morpholinylmethyl)cyclobutyl]phenyl}-1,4,5,6-tetrahydro-7H-pyrazolo[3,4-c]pyridin-7-one;

35

- N*-[(1-{4-[1-(4-methoxyphenyl)-3-(methylsulfonyl)-7-oxo-1,4,5,7-tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-yl]phenyl}cyclopropyl)methyl]-*N*-methylacetamide;
- 5 1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;
- 10 6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;
- 15 6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;
- 20 1-(4-methoxyphenyl)-7-oxo-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;
- 25 1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;
- 30 6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;
- 35 1-(4-methoxyphenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-7-oxo-

4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

5 6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

10 6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

15 1-(4-methoxyphenyl)-7-oxo-6-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl]phenyl}-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

20 6-[4-(1-{[(3*R*)-3-hydroxy-1-pyrrolidinyl]methyl}cyclopropyl)phenyl]-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

25 1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

30 1-(3-chlorophenyl)-6-{4-[1-(isopropylamino)methyl]cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

35 1-(3-chlorophenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

6-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carbonitrile;

5

1-(4-methoxyphenyl)-6-{4-[1-(4-morpholinylmethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carbonitrile;

10 1-(3-chlorophenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;

15 1-(3-chlorophenyl)-6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;

20 1-(3-chlorophenyl)-6-(4-{1-[(diethylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;

25 1-(3-chlorophenyl)-6-(4-{1-[(diisopropylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;

30 1-(3-chlorophenyl)-6-(4-{1-[(cyclopropylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;

35 1-(3-chlorophenyl)-6-(4-{1-[(cyclobutylamino)methyl]cyclopropyl}phenyl)-7-oxo-

4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-7-oxo-6-(4-{1-[(2-oxo-1-pyrrolidinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-[4-(1-{[(2-hydroxyethyl)(methyl)amino]methyl}cyclopropyl)phenyl]-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-(4-{1-[2-(dimethylamino)-2-oxoethyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-{4-[1-(methoxymethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carboxamide;

1-(3-chlorophenyl)-6-{4-[1-(methoxymethyl)cyclopropyl]phenyl}-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(3-chlorophenyl)-6-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(3-chlorophenyl)-6-(4-{1-[(dimethylamino)methyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1-(3-chlorophenyl)-6-[4-(1-{[(2-hydroxyethyl)(methyl)amino]methyl}cyclopropyl)phenyl]-



7-oxo-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

1- (4-methoxyphenyl) -7-oxo-6- (4- {1- [ (2-oxo-1-  
5 pyrrolidinyl)methyl]cyclopropyl}phenyl) -4,5,6,7-  
tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

*N*- [ (1- {4- [3-cyano-1- (4-methoxyphenyl) -7-oxo-1,4,5,7-  
tetrahydro-6*H*-pyrazolo[3,4-*c*]pyridin-6-  
10 yl]phenyl}cyclopropyl)methyl] -*N*-methylacetamide;

6- (4- {1- [ (cyclopropylamino)methyl]cyclopropyl}phenyl) -1- (4-  
methoxyphenyl) -7-oxo-4,5,6,7-tetrahydro-1*H*-  
pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

15

6- (4- {1- [ (cyclobutylamino)methyl]cyclopropyl}phenyl) -1- (4-  
methoxyphenyl) -7-oxo-4,5,6,7-tetrahydro-1*H*-  
pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

20 6- [4- (1- { [ (2-hydroxyethyl) amino]methyl}cyclopropyl)phenyl] -  
1- (4-methoxyphenyl) -7-oxo-4,5,6,7-tetrahydro-1*H*-  
pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

6- [4- (1- { [ (2-hydroxyethyl) (methyl) amino]methyl}  
25 cyclopropyl)phenyl] -1- (4-methoxyphenyl) -7-oxo-4,5,6,7-  
tetrahydro-1*H*-pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

6- (4- {1- [ (diisopropylamino)methyl]cyclopropyl}phenyl) -1- (4-  
methoxyphenyl) -7-oxo-4,5,6,7-tetrahydro-1*H*-  
30 pyrazolo[3,4-*c*]pyridine-3-carbonitrile;

5- (4- {1- [ (diisopropylamino)methyl]cyclopropyl}phenyl) -3- (4-  
methoxyphenyl) -3,5,6,7-tetrahydro-4*H*-  
[1,2,3]triazolo[4,5-*c*]pyridin-4-one;

35

- 5-(4-{1-[(isopropylamino)methyl]cyclopropyl}phenyl)-3-(4-methoxyphenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 5 3-(4-methoxyphenyl)-5-(4-{1-[(methylamino)methyl]cyclopropyl}phenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 3-(4-methoxyphenyl)-5-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl}phenyl}-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 10
- 3-(4-methoxyphenyl)-5-(4-{1-[(2-oxo-1-pyrrolidinyl)methyl]cyclopropyl}phenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 15
- 5-[4-(1-{[(2-hydroxyethyl)amino]methyl}cyclopropyl)phenyl]-3-(4-methoxyphenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 20
- 3-(3-chlorophenyl)-5-[4-(1-{[(2-hydroxyethyl)amino]methyl}cyclopropyl)phenyl]-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 25 3-(3-chlorophenyl)-5-[4-(1-{[(2-hydroxyethyl)(methyl)amino]methyl}cyclopropyl)phenyl]-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 30 3-(3-chlorophenyl)-5-{4-[1-(1-pyrrolidinylmethyl)cyclopropyl}phenyl}-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 3-(3-chlorophenyl)-5-(4-{1-[(3-hydroxy-1-pyrrolidinyl)methyl]cyclopropyl}phenyl)-3,5,6,7-tetrahydro-4H-[1,2,3]triazolo[4,5-c]pyridin-4-one;
- 35

- 6-[4-(1-{[(2-hydroxyethyl)(methyl)amino]methyl}cyclopropyl)phenyl]-  
1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-  
5 pyrazolo[3,4-c]pyridine-3-carboxamide;
- 6-{4-[1-(dimethylamino)cyclopropyl]phenyl}-1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-  
pyrazolo[3,4-c]pyridine-3-carboxamide;  
10
- 6-(4-{1-[(2-hydroxyethyl)(methyl)amino]cyclopropyl}phenyl)-  
1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-  
pyrazolo[3,4-c]pyridine-3-carboxamide;
- 15 2-(1-{4-[1-(4-methoxyphenyl)-3-(methylsulfonyl)-7-oxo-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropyl)-N,N-dimethylacetamide;
- 6-(4-{1-[2-(dimethylamino)-2-oxoethyl]cyclopropyl}phenyl)-  
20 1-(4-methoxyphenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;
- 2-(1-{4-[3-cyano-1-(4-methoxyphenyl)-7-oxo-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-  
25 yl]phenyl}cyclopropyl)-N,N-dimethylacetamide;
- 2-(1-{4-[3-cyano-1-(4-methoxyphenyl)-7-oxo-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-  
yl]phenyl}cyclopropyl)acetamide;  
30
- 2-(1-{4-[1-(3-chlorophenyl)-3-cyano-7-oxo-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-  
yl]phenyl}cyclopropyl)acetamide;

- 1-(3-chlorophenyl)-6-(4-{1-[2-(dimethylamino)-2-oxoethyl]cyclopropyl}phenyl)-7-oxo-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carboxamide;
- 5 2-(1-{4-[1-(3-chlorophenyl)-3-(methylsulfonyl)-7-oxo-1,4,5,7-tetrahydro-6H-pyrazolo[3,4-c]pyridin-6-yl]phenyl}cyclopropyl)-N,N-dimethylacetamide;
- 10 2-(1-{4-[3-(3-chlorophenyl)-4-oxo-3,4,6,7-tetrahydro-5H-[1,2,3]triazolo[4,5-c]pyridin-5-yl]phenyl}cyclopropyl)-N,N-dimethylacetamide;
- 15 2-(1-{4-[3-(4-methoxyphenyl)-4-oxo-3,4,6,7-tetrahydro-5H-[1,2,3]triazolo[4,5-c]pyridin-5-yl]phenyl}cyclopropyl)-N,N-dimethylacetamide;
- 20 2-(1-{4-[3-(4-methoxyphenyl)-4-oxo-3,4,6,7-tetrahydro-5H-[1,2,3]triazolo[4,5-c]pyridin-5-yl]phenyl}cyclopropyl)acetamide;
- 1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(2-oxo-1-imidazolidinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carbonitrile;
- 25 1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(2-oxo-1-piperazinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carbonitrile;
- 30 1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(3-oxo-4-morpholinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carbonitrile;
- 35 1-(4-methoxyphenyl)-7-oxo-6-(4-{1-[(2-oxo-1-piperidinyl)methyl]cyclopropyl}phenyl)-4,5,6,7-tetrahydro-1H-pyrazolo[3,4-c]pyridine-3-carbonitrile;